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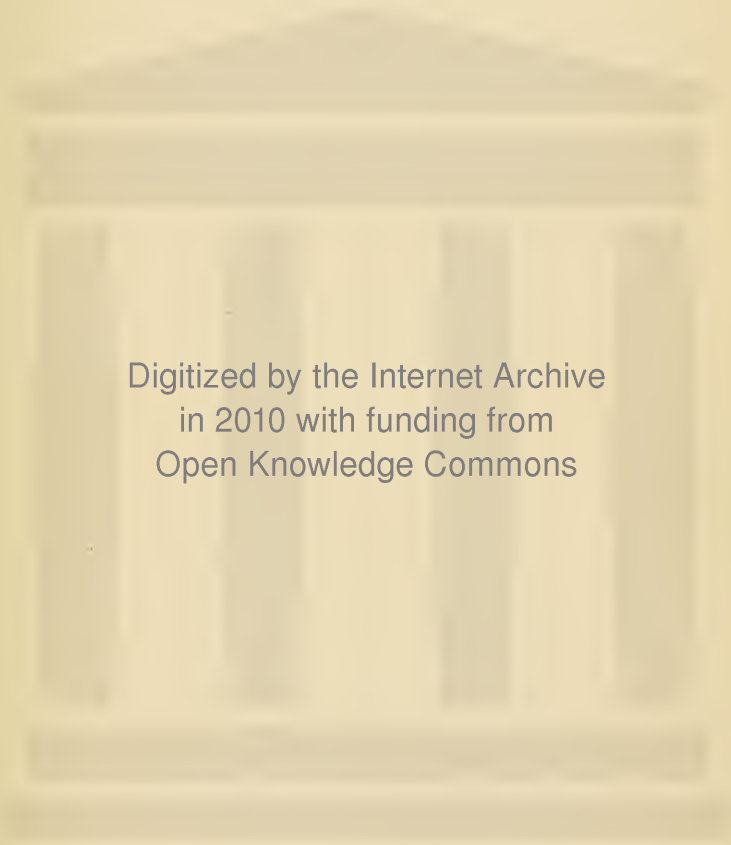
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TWENTY-FOURTH ANNUAL MEETING
OF THE
AMERICAN
GASTRO-ENTEROLOGICAL
ASSOCIATION

HELD AT THE
HOTEL BELLEVUE, BOSTON, MASS.
June 6th and 7th, 1921

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CONSTITUTION AND BY-LAWS OF THE AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION

CONSTITUTION

ARTICLE 1. This Association shall be known as the American Gastro-Enterological Association.

ARTICLE 2. The object of this Association shall be the promotion of investigation of the normal and pathological conditions of the digestive organs.

ARTICLE 3. Membership in this Association shall be of three kinds: (a) Honorary, (b) Corresponding, (c) Active.

(a) Honorary membership shall be restricted to such as have attained an international reputation by their published works and have scientifically furthered the subject of gastro-enterology. Their nomination shall take place at the annual meeting, upon the written suggestion of at least six active members and on the recommendation of the Council of the Association at the next annual meeting. Their election shall be by unanimous vote of the members present.

(b) Corresponding membership shall be restricted to foreign scientists in recognition of meritorious work within the scope of the Association. Candidates for such membership shall be proposed by at least six active members and receive the recommendation of the Council at the next annual meeting. Their election shall be by unanimous vote of the members present.

(c) Active membership shall be restricted to American and Canadian investigators and practitioners who have published meritorious work in normal or pathological anatomy or physiology, in medicine or surgery of the digestive canal and its secretory appendages, and who enjoy an unimpeachable moral standing in the medical profession.

Names of candidates for active membership must be: (1) Proposed by two active members who are not members of the Council, such proposal to be submitted to the Committee on Admissions and Ethics, which should report to the Council as soon as possible; (2) Must be recommended by the Council and (3) must receive a majority of the votes of active members present at the annual meeting of the Association.

The election of active members shall take place at the annual meeting of the Association and shall be by ballot.

It shall be the duty of the Secretary to notify active members of all nominations that are to be submitted to the Association at the annual meeting.

ARTICLE 4. The officers of the Association shall be a President, two Vice-Presidents, a Secretary and Treasurer, the latter two offices being vested in one; also three specially chosen active members to be known as Councilors, who, together with the officers, shall constitute the Council of the Association. The said Councilors shall be elected as follows: one for one year, one for two years, and one for three years.

ARTICLE 5. There shall be a Committee on Admissions and Ethics. It shall consist of the President and the Secretary and three other members, not members of the Council. These members shall be elected at the annual meeting at which this Amendment shall be adopted for the following terms: one for three years, one for two years and one for one year. At each subsequent annual meeting one member shall be elected for the term of three years to fill the annual vacancy. No member of the Committee shall be eligible for re-election until after one year shall have elapsed from the end of his term of service. It shall be the duties of the Committee on Admissions and Ethics to examine the merits of candidate, to investigate any charges made against a member, and to report the results of the examinations and investigations to the Council in writing in the shortest possible time. It shall also be the duty of this committee to study the active work in science and practice of gastro-enterology accomplished in this country and Canada and to invite the meritorious workers to join this Association.

ARTICLE 6. The election of officers, Councilors and of the members of the Committee on Admissions and Ethics shall take place at the annual meeting and shall be by ballot.

ARTICLE 7. Vacancies in the offices occurring in the interval between the annual sessions shall be filled temporarily by the Council.

ARTICLE 8. The annual meeting of the Association shall be held at a time and place to be decided by the Council.

ARTICLE 9. The President shall be the chairman of the Council.

ARTICLE 10. There shall be annually two meetings of the Council; one shall take place at the call of the President, shortly after the annual meeting of the Association; the other shall take place at least four weeks previous to the annual meeting. It shall be within the discretion of the President to conduct this latter meeting by correspondence.

ARTICLE 11. The Council shall manage the affairs of the Association in accordance with the Constitution and By-Laws, and its minutes shall be reported to the Association at the annual meeting.

ARTICLE 12. This Constitution may be amended by a two-thirds vote of all the active members at any annual meeting, provided that notice of proposed amendments has been given in writing to all the active members of the Association by the Secretary, and provided further that such proposed amendments shall have been submitted to the Council and held over for one year.

ARTICLE 13. Any member failing to attend three consecutive annual meetings without an excuse acceptable to the Council shall be dropped from the roll. The Secretary, however, shall be required to call the attention of a delinquent member to the facts in his case previous to the third meeting.

ARTICLE 14. This Association adopts the Code of Ethics of the American Medical Association. Charges of advertising, of publishing knowingly false scientific statements, of actions unbecoming a gentleman and a high standing physician, etc., shall be investigated by the Committee on Admissions and Ethics. The accused shall have liberal opportunities to clear himself of the accusation. The Committee shall report its findings to the Council, and on the recommendation of this body an offending member may be expelled by a three-fourths vote of those present at the annual meeting.

BY-LAWS

ARTICLE 1. The President and Vice-Presidents shall discharge such duties as are implied by their respective offices. The President shall preside at all sessions of both Council and Association.

ARTICLE 2. The Secretary shall attend to the usual clerical duties of the Council and Association. As Treasurer, he shall keep a record of the payments and arrearages of dues, and report on both at the annual meeting.

ARTICLE 3. The Council shall report its transactions to the annual meeting of the Association. It shall superintend the publication of scientific papers, but shall not appropriate for such printing an amount exceeding the sum of \$100, without the vote of the Association. The order of business shall be arranged by the Council before the annual meeting. It shall pass upon the eligibility of candidates for membership.

ARTICLE 4. The yearly dues of active members shall be five dollars, payable in advance. Any member whose subscriptions shall be in arrears more than two years shall be reminded of the fact by the Treasurer, in writing in event that payment be not then made he may, on vote of the Council, be dropped from the roll of the Association. It shall be the duty of the Treasurer to report all members who are in arrears to the Council.

ARTICLE 5. When sufficient money is in the treasury the membership dues may be omitted when decided by the Council.

ARTICLE 6. These By-Laws may be amended, repealed or suspended by a two-thirds vote of the members present at any meeting of the Association.

ARTICLE 7. The quorum of the Association for the transaction of business, but not for the reading of papers, shall consist of seven active members.

ARTICLE 8. All titles of papers submitted for reading at the annual meeting shall be sent to the Secretary not later than four weeks before the date of the meeting.

ARTICLE 9. A typewritten abstract of not over three hundred words, of every paper to be read, must be sent to the Secretary at least four weeks before the annual meeting. It shall be the duty of the Secretary to send to each member of the Association a complete list of the papers to be read at the annual meeting, with their full titles, at least two weeks before the annual meeting.

ARTICLE 10. Papers submitted to be read before the Association shall not have been previously published or read elsewhere. Papers shall not exceed the limit of fifteen minutes without the consent of the majority of members attending.

PRESIDENTIAL ADDRESS

JOSEPH SAILER

Philadelphia, Pennsylvania

Diagnosis is the beginning of treatment; it is, from the patient's standpoint, a means and not an end. He or she comes to the physician for cure, improvement or alleviation: and cares not, so the result is achieved, how it has been accomplished. But haphazard success is not medicine, no matter how well the patient is satisfied. The handling of a case of disease is like building a house; the builder must have the plan, the materials, the tools. The plan is the diagnosis, the knowledge of the conditions to be met; the materials, the human body to be formed into a more harmonious and efficient structure; and the tools, the methods of treatment that we employ for this purpose.

Laennec is the discoverer of rational diagnosis; for more than a century since he laid the foundation of rational physical diagnosis the medical profession, aided by biology, chemistry and physics, has wrought to make diagnosis exact, with a success that would be as inconceivable to Sydenham as the wireless and phonograph would have been to his contemporaries.

Particularly has this been true of the gastrointestinal tract. The esophagoscope, the X-ray, accurate chemical analysis of the materials obtained through tubes or discharged, the study of the relations of other organs, and the bioscopy procured by the surgical operation have taught us the existence and nature of things undreamt in the philosophies of our most brilliant predecessors. A relative accuracy is obtainable.

Has treatment kept pace? From practically nothing to the present day its advance is enormous. Aided by more exact diagnosis much is possible. Surgery is available, its results are brilliant. For some of the infectious diseases of the alimentary tract, efficient treatment has been found. Methods of treatment have been devised for ulcer and colitis, lauded by their inventors, of whose value it is somewhat difficult to reach a correct conclusion. Much harness has been devised for splanchnoptosis. Aside from these we have acids, alkalis, antiseptics whose benefits are more or less suppositions, and

diets of various complexity. Much of what is done for many of the conditions that are met is still empirical and the results have produced a class of patients, who wander from one physician to another seeking a relief that is rarely, if ever, found.

It is not possible that some of the available tools have been neglected and that a more careful study of their actions and uses might enhance our therapeutic efficiency.

Perhaps the most important elements in digestion are the ferments. If one glances at the formulas of the manufacturers of tablets or chances occasionally to read prescriptions of physicians, it is obvious, that in spite of the investigation of the physiologists, the knowledge of the conditions that are necessary for the activity of these ferments is not wide spread. The best that can be said of most of these formulas is that the ferments, as administered, are probably harmless; that they could be of any help to digestion is impossible.

Pharmacology has been of little service. What benefit pepsin and the so called pancreatin can be, other than aiding a feeble digestive action, is unknown. It is even very doubtful if they do aid digestion. This I believe is a mistake. It is possible that these ferments, properly prepared have some action on the human body in addition to their ability to accelerate so greatly the chemical changes in the food stuffs.

Some years ago Dr. Clifford B. Farr and I made some tests on all the varieties of pepsin and pancreatin that we could purchase; particularly to determine their digestive power upon egg albumin by the Mette method. The results were scanty. Some preparations were inert, some excellent. The tryptic activity of the pancreatic preparations was slight compared with the proteolysis of the pepsin preparation. The work was not published. It added nothing.

Later I observed over a period of years a case that suggested to me that the pancreatic preparations might in some cases be useful.

The patient, a woman of fifty-two years, complained of having indigestion for a year. She had cystitis at twenty-seven, and for many years arthritis pains with slight enlargement of the joints. She was a large woman but weighted only 117 pounds. She complained particularly of severe pain after eating. Her appetite was poor and she was constipated. The physical examination gave tenderness 1 inch above the umbilicus disappearing during deep inspiration, a possible sign of pancreatic tenderness; and a small mass in this region lying to the left of the spinal column. The X-ray showed a shadow in the region of the pancreas that Dr. Pancoast diagnosed a probable pancreatic calculus. The gastric acidity was always low. Carbohydrate always increased the pain and a most severe attack was caused by the administration of glucose. This produced a faint reaction for sugar

in the urine passed shortly afterwards. Two months after she was first seen, she was given pancreatin in glucoïd capsules, prepared by placing filled and sealed gelatine capsules in formalin for three minutes. The effect was surprising. The pain was controlled, the weight increased rapidly, having previously continued to fall until it reached 113 pounds, so that in one month she had gained 7 pounds and in eight months 30 pounds. She was able to eat carbohydrates freely and without discomfort. No other treatment was employed. When from time to time the pancreatin was discontinued the symptoms returned and she would lose weight. Finally, however, it was found to be no longer necessary and after six years of treatment she had apparently recovered. Thirteen years after her first visit she returned to report and to permit the first extraction of the duodenal contents. These tested for trypsin and amylolysin gave strongly positive reactions. She is apparently well.

I saw a similar case in consultation. She was placed upon the same treatment and her physician reported success.

The only conclusion to be drawn is that in a case of possible chronic pancreatitis the administration of pancreatin apparently at first relieved and ultimately cured the patient in some manner whose nature can only be surmised. But it suggests that perhaps all the physiological actions of pancreatin have not been discovered and that some of these actions may be useful in the treatment of disease. It is a field that has hitherto been avoided.

OBSERVATIONS ON *B. ACIDOPHILUS*: ITS BACTERIOLOGICAL CHARACTERISTICS AND POSSIBLE THERAPEUTIC SIGNIFICANCE

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AND

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The interest of the medical profession in intestinal microorganisms was first aroused in 1880 by the discovery and isolation of the *B. typhosus* by Klebs, Eberth and Koch. Nothing was known at that time of those organisms which have since been called the typhoid-colon group, so that when Escherich announced the discovery of the *B. coli* a distinct and important step was taken towards a lucid classification of fecal bacteria. Yet it remained for Tissier to prove that Escherich had included the *B. bifidus* with the *B. coli* and in his publication definitely differentiated these two groups of fecal bacilli. With this announcement, the Gram-positive bacilli became the subject for investigations and finally in 1900, Moro described the *B. acidophilus* giving its distinctive characteristics.

It is with this organism that our study has been carried on. Before setting forth some of the results of this work, let us briefly consider the bacterial changes in the human intestine from birth to adult life.

The meconium is sterile, but immediately after birth, becomes invaded by microorganisms. Their number, however, is never large as meconium is a poor culture medium. Nevertheless, *B. coli* have been recovered from meconium passed ten hours after birth. The intestinal flora of the breast-fed infant is predominately Gram-positive and consists chiefly of *B. bifidus* and *B. acidophilus*; *B. coli* and other bacteria are present, but in insignificant amounts. The flora of a bottle-fed infant, however, shows a goodly number of *B. coli*, *Streptococcus lacticus* and staphylococci, although *B. bifidus* and *B. acidophilus* still predominate. As soon as milk ceases to be the main constituent of the child's diet, the Gram-positive element of the

intestinal flora rapidly diminishes and *B. bifidus* and *B. acidophilus* exist only in small amounts.

In the adult, the character of the intestinal microorganisms is dependent largely upon the nature of the individual's diet. With the normal mixed diet, the *B. coli* and allied bacteria are found in high predominance, completely overshadowing the *B. acidophilus* which is often only found after a prolonged search. The adult on a milk diet, however, has a considerable number of Gram-positive *B. acidophilus* in his feces, and at times, on an exclusive milk diet, these organisms even predominate the intestinal flora.

However, the great majority of adults ingest large, if not excessive amounts of protein and the average fecal flora is composed of from 80 to 95 per cent of *B. coli* and allied bacteria. It is in these individuals that we so often find extensive intestinal putrefaction.

For years, the large intestine has been regarded as furnishing the etiological factor responsible for many diseased states and it was the trend of medical thought that in whole or in part, the absorption of bacterially-split protein derivatives was causing the premature onset of senile changes in the arteries, heart, kidney and so forth. So that when Metchnikoff in 1906 offered his Bulgarian *Bacillus* as a means of destroying the *B. coli* and thus eliminating or minimizing intestinal protein putrefaction, it was hailed with considerable enthusiasm. We know now, however, that the administration of large doses of live *B. bulgaricus* cultures does not decrease the number of *B. coli* present in the intestines of animals or man; and furthermore it has been conclusively demonstrated that *B. bulgaricus* cannot be implanted in the human intestine in spite of radical changes in the diet. But Metchnikoff's work has not been in vain and his ingenious theory has inspired others to find a means of holding in check the *B. coli* in vivo.

For some time Rettger of Yale and his co-workers have experimented with *B. acidophilus* on animals and man. They have shown definitely that this organism can be implanted in the intestinal tract and that coincident with this implantation there is a gradual decrease in the number of *B. coli* to a point where they represent 10 per cent or less of all the fecal bacteria. Their experiments with rats have also shown that this same effect may be produced by the ingestion of large amounts of lactose or dextrin.

Rettger's important bacteriological findings suggested to us a clinical study of this organism and we began administering *B. acidophilus* cultures to a number of human subjects suffering from marked chronic

constipation with its typical and well known symptoms. Encouraged by the markedly beneficial results reported to us by these patients, we then turned our attention to that large variety of intestinal disorders known as the chronic diarrheas, the results of which will be mentioned later. We will now discuss the method of administering the *B. acidophilus* cultures.

At first fermented milk was given. This was prepared by inoculating sterile milk with *B. acidophilus* and allowing it to incubate at 37.5°C. for from forty to fifty hours. Either whole or skim milk may be used. The dose is from a pint to a quart daily given preferably before meals in amounts ranging from $\frac{1}{2}$ to 1 tumblerful. This method, however, proved to be inconvenient from a practical standpoint, thereby necessitating a different means of administration. A broth culture in which this bacillus grows luxuriantly, giving the optimum concentration, was finally used.

The broth is so prepared that each cubic centimeter contains 100,000,000 *B. acidophilus* organisms and the dose is from 10 to 20 cc. either two, three or four times a day, before meals, depending entirely upon the response of the individual.

The technique of preparation of the broth is simple and is as follows:

- I. To 1000 cc. of distilled water add 4 grams Liebig's meat extract, 10 grams peptone (Mercks) and 5 grams sodium chloride (NaCl).
- II. Heat over free flame until thoroughly dissolved, stirring constantly.
- III. Titrate and adjust to required reaction; *pH* 6.9-7.0 *neutral*.
- IV. Sterilize in 1 liter flasks for one hour in Arnold sterilizer.
- V. Filter bouillon *cold* the next day through filter paper, until clear.
- VI. Add to clear bouillon, to 1000 cc. 50 grams of lactose (5 per cent) shake well, until sugar is dissolved.
- VII. Pour media in flasks, 300 cc. in 0.5 liter flasks.
- VIII. Place the flasks stoppered with cotton in the autoclave for *twenty-five minutes* and sterilize at *15 pounds pressure*.

These flasks are then inoculated and incubated at 37.5°C. for about sixty hours. They are then removed and the clear supernatant fluid is decanted. This simple procedure gives approximately a concentration of 100,000,000 bacilli to each cubic centimeter. The culture is then distributed in sterile 8-ounce bottles and kept cool until used.

In this medium *B. acidophilus* grows luxuriantly, although growth is not perceptible until the end of forty-eight hours. This fact is of considerable practical importance for it affords a simple and yet

accurate means of determining the purity of the growth. The usual laboratory contaminants, which are the *Bacillus subtilis* and *Staphylococcus albus*, show a luxuriant growth in this medium at the end of twenty-four hours. Furthermore, these contaminants are more or less evenly distributed and the contaminated flasks show a uniform density. The growth of *B. acidophilus*, however, is a thick, heavy, slimy growth which settles quickly to the bottom and leaves a clear supernatant layer of bouillon above. Thus the contaminated flasks are easily detected and thrown aside.

The *B. acidophilus* is Gram-positive, varying in shape from short to long rods. On lactose agar it forms small whitish-gray colonies with wavy margins. It grows slowly, being hardly perceptible at the end of twenty-four hours. This organism ferments milk, producing acid slowly so that the milk does not usually begin to sour until incubated for about thirty to thirty-five hours.

Recently, in the preparation of this broth, sodium phosphate instead of sodium chloride has been used. This salt acts as a buffer, and by neutralizing the acid formed, will, we believe, increase the length of time of viability of the culture. This work, however, is still incomplete.

In carrying on this clinical study, *B. acidophilus* cultures were first administered to individuals whose only obvious ailment was chronic constipation. These patients have been under constant observation for a period covering five months or less. Only cases of the severest type were chosen, and particularly those of many years standing. In a short time these subjects experienced considerable relief and maintained, while on the treatment, a state of excellent health. The following is an illustrative case:

The patient, a male, fifty-two years of age, a professor in Yale University, had been constipated since boyhood. For twenty years he has never had an action of the bowels except by means of cathartics, which were taken daily. He has been troubled with repeated attacks of erythema multiforme and at one time had a persistent eruption which was finally found to be due to phenolphthalein. Has worked hard, but latterly felt his ambition waning without actually being ill. His urine was loaded with indican and the stools were dark, very foul and filled with colon bacilli. January 18, 1921, he was put on *B. acidophilus* culture in 2-teaspoonful doses, four times daily and all cathartics stopped. For three days he had no action of the bowels; then there was a copious stool, and since then there has been a normal daily movement. The stools are yellow, formed and inoffensive. Indican has disappeared from the urine. This man states that he feels better than he has for a long time.

Of 50 cases of chronic constipation, 42 gave satisfactory results. Of the chronic diarrheas, again only the severest cases were employed, and to date, 10 cases out of 12 have shown marked improvement. These individuals have been under constant observation ranging from three to five months.

The following is an illustrative case of mucus colitis of six year's duration:

A woman of forty-three years of age has had painful intestinal contractions with the evacuation of large quantities of mucus, which at times has been blood streaked and diarrheal in character. This patient was distinctly neurotic and had gone the rounds from osteopathic, chiropractic and allopathic practitioners. She was given the numerous treatments recommended without much relief, and finally was placed upon *B. acidophilus* treatment early in February of this year. At first there was an increase of her bowel movements but the treatment was persisted in and after the first week, regular formed bowel movements began and have continued up to this time, accompanied by relief of her pain. The blood has entirely disappeared from her stool.

Bacteriological and microscopical studies of the feces have been made on patients and show the same changes as Rettger demonstrated. Before treatment, the fecal flora showed Gram-negative bacilli (the *B. coli* group) in huge predominance, often representing 90 to 95 per cent of all fecal organisms. From two to three days after the beginning of the administration of *B. acidophilus* cultures by mouth, they are first demonstrated in the stool. From that time on they increase in number until on the fifth or sixth day they represent about 90 per cent of the fecal microorganisms. At the same time there occurs a proportionate decrease in the number of *B. coli* until they are present as less than 10 per cent of all the intestinal bacteria. From the sixth day on, while the culture is being taken, the fecal flora consists predominately of Gram-positive rods, regardless of the character of the individual's diet.

When the administration of the culture ceases, the *B. coli* begin to increase, slowly at first, until the fifth or sixth day, at which time they again are present as the predominant type of bacteria. If, however, lactose or dextrin is included in the diet, this transition may be retarded considerably.

As the change from Gram-negative to Gram positive flora takes place, there occurs a change in the physical characteristics of the feces. The fecal masses become larger, softer, lighter in color, and comparatively odorless, while evacuation is unattended by gripping

pains. The stool, moreover, is usually formed, regardless of the amount of the culture ingested.

The work of Rettger mentioned above, has opened up a large field for investigation. In this paper we are reporting the results of a small clinical study. The results are highly satisfactory and we hope to continue work along similar lines. The therapeutic properties of *B. acidophilus* are still in the experimental stage, but it is safe to say that the value of this form of treatment promises much hope for the future. Serious consideration should also be given as to the best methods to be employed for its administration.

However, as a result of this study we feel justified in drawing the following conclusions:

1. *B. acidophilus* when given by the mouth can and does implant itself in the intestinal tract.
2. The administration of *B. acidophilus* is accompanied by a marked decrease in the number of *B. coli* in the feces and the supplanting of these by the *B. acidophilus*.
3. In chronic constipation there was marked improvement from the so-called toxic symptoms and relief from the constipation which coexisted.
4. In the chronic diarrheas there was an abatement of the symptoms.

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DISCUSSION

DR. THOMAS R. BROWN, Baltimore: I should like to say how much interest I have seen taken in the importance of this paper from men who have visited New Haven. These men were all impressed with the value of this work. I should like to ask Dr. Gompertz and Dr. Vorhaus whether they ascribe the beneficial effects from the use of lactose in toxic manifestations; and, second, whether the great increase of the *bacillus acidophilus* which follows the administration of this is responsible; and, third, whether they have attempted to prepare the bacillus in tablet form and whether it retains its cultural characteristics in these cases.

DR. MARTIN G. VORHAUS, New York: There are just a few points which I would like to emphasize in the paper just read by Dr. Gompertz, and one is about the method of administration of this organism. We used the fermented milk and also the broth culture. It might be well to compare the merits of these two preparations. The fermented milk contains a large number of living organisms, and for that reason is considered the most valuable method of administration. But it was found impracticable because the patient had to come daily to receive this fermented milk, and a large number of individuals found this liquid milk unpleasant to take, and for that reason and for the fact that the milk, if kept in a warm place, spoils, we prepared the broth culture. The culture may contain a smaller number of organisms, but we found from a clinical experience and examination of the stools that implantation took place just as quickly as from the milk preparation, and the clinical results were just as good. The examinations of the stools were made by the usual bacterial plating method and by staining the organisms by Gram staining. We felt it always advisable to control always on the same slide as there was quite an individual equation in preparing these slides. We found in the transition that the Gram-positive *B. bacillus* took place just as effectively from the broth culture as from the milk preparation. We hunted up to find a means of determining whether putrefaction was being minimized and early in the work we felt it advisable to discard the indican test as being of doubtful value. We believe that the determination of the ethereal sulphates in the urine is a more reliable method, but the quantitative tests on these are as yet unsatisfactory.

DR. FRANK SMITHIES, Chicago: I do not wish to take much of the time of the Society, but I feel that there should be some discussion of this subject. Thanks to Dr. Gompertz, we were able to receive some of these cultures a few months ago. Our experience is limited to the treatment of 5 cases of chronic diarrhea, in association with gastric achlorhydria. I think it is very important to emphasize the fact that one should have a fair knowledge of what is in the stools before he starts the administration of the *B. acidophilus* preparations; even though clinical symptoms may improve, as frequently occurs periodically in some of these patients, yet it will not be possible to have any control, as to the value of these cultures in changing fecal flora unless there has been previous knowledge of the normal variation (for the given individual) of the stool, with respect to bacterial content, "putrefactive products" and undigested food, unless careful stool examinations have been made over a sufficient period before the special therapeutics is begun. It seems to us that we only got results after thorough saturation of the stool with *B. acidophilus* and after this has been secured it does not seem necessary, constantly, to give great quantities of this preparation; when stool analyses show that the *acidophilus* is again in the minority, one can again begin the administration of broth cultures. Sometimes patients complain that the preparation (the broth culture), is disagreeable to smell and to taste. We suggest that in hospitals or at clinics, its administration once daily, in at least 1-ounce dose, directly into the duodenum through the Rehfuess duodenal tube. We feel that such procedure is well worth consideration.

Our 5 cases have improved, since we began using Dr. Gompertz's preparation. In 2 of them we believe that improvement has been more satisfactory than by any other mode of treatment with which we are familiar.

It is important that one should remember that the administration of *B. acidophilus* is not the only thing to be done for this special group of patients. The patient has to be treated from all other viewpoints; one must not rest content to give merely a tablet or some broth to the patient and then send him away. He has to be treated rationally from other standpoints, namely, with respect to infection extraneous to the bowel lumen, with regard to secretory or anatomic anomalies, faulty dietary, anemia, habits, etc. If this be not done, then the mere altering of the bacterial flora of the gut will not be productive of the greatest good.

DR. LOUIS M. GOMPERTZ, New Haven (closing): In answer to Dr. Brown's question we believe that the lactose in the broth has very little effect, as it is present in only about 1%. With the milk preparation however, large amounts of lactose are used, and this may have a lot to do with the increased efficacy of the milk in constipation, for example.

Now as to the tablet form—we have not tried that as yet. I presume there will be lots of preparations on the market. We are afraid that when it is put on in other forms that it will not be as efficacious as the broth preparation.

A microscopic and bacteriological examination of the stools was made in the large number of cases by Dr. Vorhaus, who has been doing most of the bacteriological work.

As to the duodenal administration—that is something that should be worked out. We have tried it in a few cases by rectum, but it was difficult to control patients, and also we did not think our results were any better than when we gave our culture by mouth. The implantation takes place just as well by mouth as by rectum. But the duodenal method of giving it I think is something that should be tried, and I thank Dr. Smithies for the suggestion.

VISCERAL ADHESIONS AND BANDS: NORMAL INCIDENCE, A PRELIMINARY REPORT¹

JOHN BRYANT

Boston, Massachusetts

The material which is the basis of this paper was obtained before the world war incidental to a much more comprehensive investigation into the etiology and treatment of the chronic intestinal invalid. Its presentation has been delayed for several years, but there does not in the meantime appear to have been published any data which considers the question of visceral adhesions or bands from the same points of view.

The literature upon adhesions which is based upon reported facts, is scanty, contradictory, and inadequate. Although early writers frequently mentioned the existence of adhesions or bands within the abdomen, modern scientific literature upon the subject may be said to date from the exceedingly instructive paper by Virchow (5) written in 1853. Virchow not only discussed the question of adhesions in the adult, but recognized that such abnormalities were occasionally found in the fetus, and referred to the fact that some of his contemporaries or predecessors had attributed these variations in the fetus to intra-uterine peritonitis. Since the time of Virchow, however, surprisingly little in the way of accurate data has been presented, the majority of recent writers having considered adhesions largely from a surgical point of view, and even then usually on the basis of personal opinion rather than of published facts.

One of the most valuable of such papers from the surgical point of view is that by Morris (1) in which although no actual data is given, he divides adhesions into four groups in the following order of frequency: gall-bladder, cecum and appendix, sigmoid, and pelvis. Robinson (3) in 1896, reported observations based upon a variable number of cases from 40 to 150, tending to show that the viscera most frequently involved were, in their order of frequency, the spleen,

¹Original data for this article obtained in 1912-1914 through the courtesy of Professors Pick and Von Hansman of Berlin, Professor Fraenkel of Hamburg, and the students then working in their Pathological Institutes.

mesosigmoid, pelvis, cecum and appendix, and gall-bladder. Opitz (2), reporting upon a series of 160 cases examined in 1914, agreed in general with Robinson, placing the sigmoid first in frequency, followed in order by the cecum and appendix.

There are also available a few studies of special areas, again mostly from a surgical point of view, of which by far the most reliable is the recent one by Smithies (4) reporting gall-bladder condition in a series of 1000 operative cases. In general, it may be said however that there has been practically no serious attempt made to study adhesions from the point of view of sex and progressive age, or from the point of view of the normal occurrence of adhesions in unselected material.

It is believed that the present paper will to some extent supply this deficiency, since it is based upon a series of over 1000 observations upon 297 unselected consecutive postmortem cases of all ages and both sexes, the only cases excluded being those few recently postoperative, or those exhibiting recent frank peritonitis.

In the obtaining of the original data, on the one hand every attempt was made to secure accuracy, the original notes on one case being written immediately after the completion of the examination and before proceeding to the examination of any subsequent case. On the other hand, attempt was made not to overlook any variations from the accepted normal.

The data having been obtained, it was next divided for purposes of study into male and female groups. After further study, these groups were again subdivided into age periods as follows: fetal, birth to two years, two to ten years, every decade from ten to seventy years, and a senile group composed of those cases seventy years of age or over. Although when thus subdivided, the number of cases in each age group averaged only about 20, being from this point of view unsatisfactorily small, yet it was possible from this original subdivision to observe certain general tendencies which were largely substantiated by dividing the male and female groups into only four sub-groups. These sub-groups were: fetal, birth to forty years, forty years to senile, and senile. At later stages of study, these four groups were again frequently condensed into two: the group below forty years of age and the group above forty years of age.

It has been generally considered that where adhesions are found in the fetus, they are the exception and not the rule. This is not correct, and even recent attention which has been given the question of developmental bands fails to take into consideration the extreme

frequency with which such abnormal adhesions or bands occur within the fetal abdomen.

A careful study of the data available showed that there were only 8.9 per cent of 180 male cases of all ages, in whom adhesions were absent; in other words, adhesions were present in 91.1 per cent of these 180 male cases. In this male group, there was a total of 65 different adhesions or bands. Examination of the male fetal group showed that 100 per cent of 18 cases presented abnormalities; in other words, no male fetus was free from some form of abnormal adhesion or band.

In the female group of 117 cases of all ages, there were but 14.5 per cent in whom adhesions were absent; in other words, adhesions were present in 85.5 per cent of these cases. In this female group, there was a total variety of 57 different adhesions or bands. Examination of the female fetal group showed that adhesions were absent in only 12.5 per cent of 16 cases; in other words, adhesions were present in 87.5 per cent of these female fetal cases.

An examination of the total number of structures involved according to age, showed that there was practically no increase above the fetal rate in either sex until the age of forty years. In the male fetus there was an average of 3.2 viscera per case involved; in the female fetal group the average involvement was 2.9 organs per case. The actual percentage increase above the fetal rate in the male until the age of forty years was nil; in the female, under the same conditions there was an increase of only 3.4 per cent above the fetal rate. This contrasts markedly with an increase of 43.8 per cent above the fetal rate for the number of structures involved in the males of over forty years of age, and with an increased involvement under the same conditions in the female of 51.7 per cent.

The actual number of variations, in type of adhesions present in relation to the given age periods, shows a striking similarity to the figures just quoted, with the single exception that the sudden increase occurs in the thirty year decade rather than in the forty year decade. In other words, in both sexes below the age of thirty, less than 12 different types of adhesions were found in any one age group in either sex, the number varying only one or two points from the fetal rate. Above the age of thirty on the other hand, there is in both sexes a striking increase of almost 100 per cent in the variety of adhesions present, and this increased variety tends still further to increase up to and including the senile group.

The complexity of adhesions present, or in other words the number of structures involved in any given adhesive process, shows an interesting relation to age, and the general variation runs uniform in both sexes. There is from the fetus onward a progressive decrease in the number of simple adhesions present in any age group; on the other hand, there is a progressive increase with increasing age in both sexes, in the percentage of complex adhesions to be found in any given age group, from fetal to senile.

The actual adhesions or bands present show a most interesting uniformity in both sexes, not only in the fetus but in older ages, as regards percentage frequency. The order of frequency in 297 cases of both sexes, for the seven most frequent actual adhesions, is shown in table 1.

TABLE 1

Actual adhesions or bands present; percentage frequency, both sexes

ADHESIONS OR BANDS	MALE	FEMALE
	<i>per cent</i>	<i>per cent</i>
Gall bladder to duodenum and transverse colon.....	25.6	24.8
Gall bladder to transverse colon.....	17.2	9.4
Gall bladder to duodenum.....	15.5	17.9
Appendix to peritoneum.....	15.0	5.9
Omentum to ascending and transverse colon.....	11.1	12.0
Ascending colon to transverse colon.....	10.6	5.9
Duodenum to peritoneum.....	6.7	10.3

Study of the fetal groups shows that in both sexes the adhesion most frequently occurring is the same as that at the top of the list in table 1; in other words, gall bladder to duodenum and transverse colon. The second most frequent adhesion in the fetus of both sexes, is that of the gall bladder to the transverse colon. It therefore seems reasonable to assert that these two most frequent adhesions are in both sexes of congenital or developmental origin, presumably existing as unabsorbed portions of the free edge of the lesser omentum, or ligamentum hepatico-colicum.

A consideration of the location of adhesions from the point of view of the four quadrants of the abdomen, shows that not only in the fetus but in all older age periods in both sexes, the right upper quadrant is by far the most often involved. The right lower quadrant and then the left upper quadrant follow next in order of frequency.

A consideration of adhesions from the point of view of the individual organs involved at varying ages in both sexes, is reserved for a later presentation.

CONCLUSIONS

1. The frequency of occurrence of adhesions or bands in the fetus of both sexes has been greatly under-estimated. Of a group of 34 fetal cases of both sexes, only 5.9 per cent were free from demonstrable adhesions or bands; 100 per cent of the 18 male feti showed such variations from the normal.

2. The adhesions present in the fetus are less varied in number, and of a definitely less complex type than those found to occur in later life.

3. The age of forty is critical in both sexes. There is practically no increase in frequency above the fetal rate of involvement for the different viscera by adhesions, until the age of forty. Beyond the age of forty, there is a sudden increase of about 50 per cent in the involvement of the different viscera by adhesions in both sexes, the increase being somewhat more marked in the female than in the male.

4. The two actual adhesions or bands found to occur most often in both sexes at all ages, are in their order of frequency, as follows: first, gall bladder to duodenum and transverse colon in both sexes; second, gall bladder to transverse colon in the male, and gall bladder to duodenum in the female. In both the male and female fetus the two adhesions or bands most frequently found, were: first, gall bladder to duodenum and transverse colon; second, gall bladder to transverse colon. It would therefore appear that these two most frequently occurring adhesions or bands are of congenital or developmental origin.

5. The regions or quadrants of the abdomen most frequently involved by adhesions or bands in both sexes are, in their order of frequency, as follows: right upper quadrant, right lower quadrant, left upper quadrant, left lower quadrant.

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- (3) ROBINSON: *New York Med. Jour.*, 1896, lxiii, 101.
- (4) SMITHIES: *Jour. Amer. Med. Assoc.*, 1918, lxxi, 1804.
- (5) VIRCHOW: *Arch. Virch.*, 1853, v, 281.

DISCUSSION

DR. CHARLES STOCKTON, Buffalo: This paper is interesting, and it seems to me that it is of great importance. Dr. Bryant as I understood him, did not designate these as inflammatory adhesions, but as congenital anatomical conditions. My conception of an inflammatory adhesion is of one that tends to eventual disappearance, and I have evidence of such disappearance in certain instances where one laparotomy followed another. What I would like to learn from Dr. Bryant is what happens to these congenital adhesions from the period just after birth up to thirty years. The doctor did not say much about what changes occur in that intervening period. Do these adhesions continue all through life? I assume that they sometimes do, and probably his observations on that matter he can give us. Or is there disappearance of these early adhesions, as may occur in cases of ordinary inflammatory adhesions? If it is true that there are abnormal anatomical adhesions or bands that occur in the fetus and persist through life in such a large proportion of people, it certainly is time that surgeons recognized the fact.

DR. JOHN BRYANT, Boston (closing): I have a number of statistical graphs here which I think answer the questions asked. It was intended to incorporate them in my paper but circumstances prevented. I think they cover variations in relation to the different age periods. I also have a number of graphs which cover the frequency of adhesions about the individual viscera at the various age periods.

X-RAY EVIDENCE OF ABDOMINAL SMALL INTESTINAL STATES EMBODYING AN HYPOTHESIS OF THE TRANSMISSION OF GASTROINTESTINAL TENSION

R. WALTER MILLS

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There seems to have been no considerable effort made to investigate small intestinal normal or abnormal conditions by means of the X-ray, this with the exception of lesions of the duodenum which are not included in this presentation. Certain observations as to fundamentals in small intestinal motility have been recorded. The outlines suggesting gross obstruction are recognized. The strikingly apparent dilated and ribbed loops of the obstructed small intestine made visible on the plate by gas and fluid or apparent after barium ingestion have been described. Several authors have written of the very valuable information derived by the X-ray in pathological jejunal and ileal obstructive states of various etiology including congenital bands with resulting kinks. It is remarkable that so little has been done towards investigating disturbances of the small intestine, the most essential and indispensable part of the alimentary tract. With the exception of gastro-jejunal ulcer there does not appear to have been any conception that direct evidence or involvement of the small intestine might be obtained as in the instance of stomach and colon or any effort made to elicit evidence of impairments of its function other than in the instance of ileocecal valve incompetence and ileal stasis. Even the atypical segmented shadows of the organically involved small intestine have been regarded only as evidence of slight local obstruction.

For the past ten years it has been my custom to write a formal report of each X-ray examination, partly for purposes of cross-filing. Any X-ray findings not understood were systematically recorded in this report. Among other captions in this cross file was that of atypical small intestinal loops. I was thus forced to observe and make note of any small intestinal forms that were at all unusual. It gradually became apparent that certain of these forms were associated with certain conditions (tables 1 and 2); for instance that in colonic obstruction a certain form of small intestine suggesting overdistension was

generally present. This naturally led to the idea of recoil or relative stasis which conception once entertained was found to be supported

TABLE 1

Incidence of atypical small intestinal forms in series of 5735 subjects due to organic conditions

A. In organic conditions primarily involving small intestine	
General abdominal carcinomatosis and metastatic carcinoma.....	18
Tubercular peritonitis.....	5
Peritonitis and resulting adhesions of other than appendix origin.....	44
Meckel's Diverticulum.....	1
Peritoneal irritation (peritonitis?).....	2
	70
B. Where a secondary result of organic conditions	
Of cecum-appendix origin.....	142
Post operative conditions after appendectomy.....	73
Carcinoma of colon.....	14
Colitis.....	8
Diverticulosis and diverticulitis.....	11
Colonic inhibition stasis, post operative.....	1
Hirschsprung's Disease.....	1
Extra-alimentary tumor pressure.....	43
Hernia.....	16
Redundant small intestine.....	1
	310

TABLE 2

Incidence of atypical small intestinal forms in series of 5735 subjects due to functional conditions

Constipation.....	43
Achylia.....	8
Over-fluidity.....	14
Over-prompt gastro-enterostomy stoma.....	1
Debility (asthenia).....	4
Ascites.....	9
Indeterminable.....	77
	156

by collateral evidence on every hand; the same for organic conditions. These atypical small intestinal outlines were first noticed and recorded

in 1916. In the subsequent five years they have been observed approximately 600 times in the X-ray examination of 6000 persons naturally with growing frequency as they became better appreciated. For instance in the past six months 205 times in the examination of 750 patients (table 3).

A factor that was fortuitous was that in efforts to determine the exact time of complete gastric emptying for a special study of gastric motility a large series of cases were plated with the patient standing which naturally gave a filled small intestine without considerable pressure artefacts such as result when the plate is taken with the patient prone as is generally done; such plates being consequently non-informative as to the evidence to be mentioned. It is this accidental factor more than all others that accounts for my own findings which have not been

TABLE 3

Incidence of atypical small intestinal forms

A. As recorded in series of consecutively examined subjects during past five years

Number of subjects.....	5,735
Number of atypical small intestinal forms.....	536
Percentage of atypical small intestinal forms.....	9.3

B. As recorded in series of consecutively examined subjects during past six months

Number of subjects.....	752
Number of atypical small intestinal forms.....	205
Percentage of atypical small intestinal forms.	27.2

apparent because not available to others whose plates were taken with the patient prone.

The subject is difficult to present in abstract form as to functional disturbances because complicated and resting on certain unrecognized principles, perhaps more safely hypotheses, evidence supporting which it may be frankly admitted is as yet to a degree inferential and will only be possible of proof or disproof by prolonged observation. It is thus realized that suggestions to be offered are not proved and so radical that I have hesitancy in presenting them without further investigation. They seem, however, so appealing and supported by so much evidence that they are submitted to you for consideration and it is hoped will result in your investigation of them.

Since the plate itself is the most effective means of demonstration, a statement in proposition form will be given of matter to be presented

so far as possible each point illustrated by a print or two with accompanying descriptive legend.¹ It has been disconcerting that my efforts to demonstrate these atypical small intestinal forms to others have not been particularly successful. Roentgenologists of widest experience in gastro-intestinal work were unable to appreciate or differentiate outlines that to me seemed perfectly apparent and that I have every reason to believe we are utilizing daily with diagnostic helpfulness. I must conclude that appreciation of such evidence is a matter of experience and education; that one must become as it were sensitized to changes in outlines that at first are not apparent. Each of us has had a similar experience in our gradual education in the matter of duodenal cap deformity, appreciation of gall stone shadows, and so on.

We have little knowledge of factors governing small intestinal motility. A few seemingly well-founded observations and ideas are current in the literature. That the stomach is the chief regulator of the rate of small intestinal motility; that the rate of motility in the jejunum is very rapid, periodic and segmental, and that ileal motility largely lacks these characteristics; that the rate of motility progressively decreases from the duodenum to the ileocecal valve. Certain conceptions of a small intestinal segmenting peristalsis founded chiefly on observations on animals have been presented. Such action seems not so evident, at least difficult of observation in man. The function of the ileocecal mechanism has been differently understood. One teaching is that it essentially prevents a too rapid flow of small intestinal contents into the cecum. The other is that it prevents the reflux of cecal contents into the ileum. My own idea is that it more particularly functions in the latter manner though as has been taught it doubtless has a dual function, the valvular mechanism preventing reflux and the muscular action in the terminal ileum moderating proximal flow.

The small intestine bears the same relation to bodily habitus as does the stomach and colon as to form, position, tonus and motility. In sthenic types the arrangement of the whole is higher, the coils are more discrete, of different arrangement, a demonstrably greater degree of tonus and a more rapid rate of motility than in asthenic and hyposthenic subjects. There are suggestions that intra small intestinal tension is greater in sthenic types. Under normal conditions the appearance of the small intestine on the plate is characteristic judged on the basis of physical type.

¹ The illustrations of this article appear with the article as published in *The American Journal of Roentgenology*, Vol. IX, No. 4, April 1922, pages 199-223.

X-ray evidence of organic small intestinal lesions may be summarized in a word. Any organic process involving the small intestinal wall either primarily or secondarily will modify the X-ray shadow of the contents of the part involved and thus render direct diagnostic evidence of its presence; if not as strikingly as in the instance of stomach and colon or as yet as suggestively as to the nature of the lesion, none the less positively as to an organic pathological process being present.

The following principles concerned in abnormal functional small intestinal conditions may be offered. The first of these is thoroughly recognized and accepted by all of us, the others are not and must as yet be considered hypothetical.

1. When there is organic alimentary obstruction there will be dilatation and motor delay proximal to it, their degree determined by that of the obstruction and the resulting proximal dilatation or hypertrophy. Duodenal ulcer obstruction and its results on stomach form and motility is the commonest instance. To repeat we are all perfectly familiar with this principle, illustration is hardly necessary. It is unrecognized, however, and of greatest interest that in other portions of the alimentary tract impaired motility and dilatation resulting from obstruction may often be recognized in lesser degree far proximal to the obstructive point and immediately proximal area of frankly apparent motor delay. To illustrate: Obstructive carcinoma of the colon results as we all recognize in an immediately proximal dilatation and colonic motor delay, but it seems also that this dilatation is reflected proximally in diminishing degree throughout the entire colon, is especially noticeable in the appendix and is apparent in the form of the small intestine suggesting distension as a result of recoil or relative stasis and may perhaps be reflected as far as the stomach. In addition there is usually present small intestinal gas which while not to be regarded *per se* as pathological, nevertheless usually is and does not seem to occur under what may be termed admirable conditions.

It is indeed a question whether delayed progress in the small intestine may not result in impaired gastric motility. It is conceivable that such might occur as the result of inhibition of those stimuli that result in expulsive activity on the part of the stomach as does occur in much greater degree in acute small intestinal obstruction. My attention was attracted to this possibility some years ago in attempting a study of causes of delayed gastric emptying. In that study certain conditions such as chronic appendicitis and gall-bladder disease were found suggestively associated with slow gastric emptying. Thus 15.4

per cent of a considerable series of cases of chronic appendicitis and 34 per cent of a series of gall-bladder disease showed six hour residues on a standard contrast meal; rather a course test considering variability in the time of complete gastric emptying in different types of individuals. The cause of this was not apparent and the study thrown aside in the hope the reason would later be found. The present effort is partly the result of attempts to reach a solution of the problem. Certainly on clinical grounds the explanation of the functional dyspepsias associated with organic surgical and possibly functional non-surgical conditions such as constipation partly on the basis of slow gastric motility would seem attractive. This might result through inhibition secondary to distal small intestinal motor delay or inhibition of proximal (gastric) motility as in gall-bladder disease. One might even conjecture that biliary motility was influenced in some such fashion, i.e., that slow biliary flow was secondary to small intestinal hypomotility in turn the resultant of colonic stasis. Clinically again there are suggestive things. For instance the insistence of certain persons on the cure of their "biliousness," whose explanation no physician may attempt, by means of purgatives which we are thoroughly assured are not cholagogue but which apparently amply serve the end desired from the patient's standpoint.

2. Evidence strongly suggests that the same far reaching proximal recoil occurs in somewhat less degree in functional stasis of the colon as is marked colonic constipation. The X-ray apparently shows that not only is there resulting motor delay throughout the entire colon but also secondarily in lesser degree in the small intestine. Such evidence of small intestinal recoil through the form of the small intestinal loops as resulting from constipation naturally does not differ from that indicating the secondary effect attributable to slight or moderate colonic obstructive states. It has been taught that there is no constipation of the small intestine; there is not on the same time ratio, but recall the comparatively rapid motility of the small intestine. Interestingly the fact that it is thus less evident suggests too a greater peristaltic energy on the part of the small intestine with consequent greater tension within it. The ileum can drive its contents into an over-filled even obstructed cecum without great delay; a suggestive idea of many leads and bearings, especially as to whether colonic contents regurgitate or reflux into the terminal ileum under natural conditions as in the case of the barium enema.²

² I have since learned that Case has definitely determined this to occur.

3. Any alimentary sphincter that is subjected to increased intravisceral tension originating either immediately proximal or distal to it tends to give way and if this tension is sufficiently great the sphincter becomes divulsed and incompetent, dilates in common with the contiguous dilated gut with resulting disturbance of proximal and distal motility. An illustration of the first condition is afforded in the gaping incompetent pylorus occurring in certain cancers of the stomach, the expression of its divulsion resulting from increased intragastric tension in turn the product of decreased intragastric capacity, lessened elasticity of the stomach walls and stomach elevation in toto, favoring over-rapid emptying through gravity. This latter statement made advisedly. Obstruction of the distal duodenum resulting in dilatation of the duodenum proximal to it and of the pylorus and of the stomach in common, is an illustration of the second. In the first instance that of the gaping incompetent pylorus resulting from contracting cancer of the stomach, distal motility is abnormal—over-rapid largely because the controlling sphincteric action of the pylorus is lost as a result of the factors mentioned. In the second instance that of an obstruction of the distal duodenum with secondary divulsion of the pylorus, proximal motility of not only the duodenum but the stomach as well is interfered with. The pylorus being divulsed duodenum and stomach become one ventricle. Less spectacularly but just as truly, the same dynamics obtain in the instance of every other alimentary sphincter, the cardia, ileocecal mechanism and rectosigmoid.

Ileocecal valve incompetence is as has been contended not essentially a thing of the moment effected by barium enema pressure, but instead the reflux of the enema into the terminal ileum expresses its actual acquired and constant relative incompetence, the result of persistent increased intracolonic tension beyond from various causes, most commonly constipation usually contributed to by an inherently low degree of sphincteric tonus as occurring in asthenic states. It is a result and not a cause. The whole subject of ileocecal valve incompetence and ileal stasis as written of by clinicians and roentgenologists is full of suggestions of acquired patulence and secondary small intestinal recoil without the situation apparently being appreciated. Incidentally reflux through the ileocecal valve of the barium enema does not necessarily mean that the same thing occurs under natural conditions though it usually indicates an acquired patulency. The result is but the expression of the balance between the artificial pressure exerted and the resistance offered. Even under perfectly normal con-

ditions the small intestinal column must feel the resistance of the cecal contents ahead at those times when the sphincter mechanism in the terminal ileum is open. It is only when distal resistance is abnormally great through abnormal conditions and a certain maximum pressure is exceeded that the valve gives way. The whole present conception of abnormal intra-alimentary tension transmission points to one function of the sphincters being that of protectors or guards against pernicious transmission of tensions in addition to the usually appreciated action of favorably retarding motility that the ends of digestion and absorption may be served. The function of the pelvirectal sphincter is to prevent the forming stool from entering the rectum which is normally empty excepting just before defecation, the urge to which is excited by the descent and presence of feces in it. As has been determined by my associate, Soper, through sigmoidoscopic studies, the majority of cases of constipation are concerned either with loss of contractility of the pelvirectal sphincter or its overtonicity. In the first case secondary to its divulsion through constant rectal accumulation of feces in turn caused by ill habits and habituation of the rectum to such fecal presence and by the constant abuse of purgatives exposing the sphincter to frequent unnatural strain. In the second spasticity of the pelvirectal sphincter and contiguous pelvic colon result in proximal fecal retention.

4. Any acquired local lack of resilience in the gut wall as from an inflammatory or other pathological condition will lead to recoil and relative proximal stasis. A sclerosing duodenal ulcer even if it does not actually involve and result in fixed contracture of the pyloric sphincter is frequently associated with a slight or moderate delay in gastric motility—a six-hour residue and a degree of gastric dilatation. This may be an expression of final fatigue on the part of the stomach walls from the ulcer resistance offered in the cap, whose function would thus be suggested as that of a shock absorber for gastric peristaltic impulse.³ In such a duodenal ulcer the pylorus itself is often shown by the plate to be actually open and roentgenoscopically to be incompetent, divulsed by the increased intragastric tension instead of in spasm,

³ The size and form of the duodenal cap indicates the extent to which it is subjected to pressure—plus its form and direction and the influence of the essential degree of visceral tonus of that person. Where the pylorus is patulous and the cap vertical it will as a rule be large. In heavy hypersthenic persons with high hypertonic stomachs the cap is non-retentive because its downward direction favors non-retention through gravity. It will consequently be small and not apparently greatly differentiated.

usually considered the causative factor in the delayed gastric emptying. It may even be that the secondary indications, the indirect signs of non-obstructive duodenal ulcer, can be accounted for on the basis of abnormal distal resistance. The hyperperistalsis as the direct response; the initial hypermotility as the resultant of hyperperistalsis thus excited plus the incompetence of the pylorus to a degree divulsed through increase in intragastric tension. A stomach not regularly distended tends to contract as in starvation or when the patient is on a soft diet. The gastric hypertonus may thus represent lack of gastric distension, the product of hyperperistalsis and initial hypermotility. A cecum whose elasticity has become impaired as a secondary result of an old appendicular inflammatory process or which offers increased resistance through malposition or even a retrocecal appendix will practically always be associated with an atypical form of small intestine indicating relative stasis as the result of recoil from the increased cecal resistance beyond. Clinical medicine furnishes a number of illustrations of the untoward results of abnormal modifications of intravisceral tension of great practical importance. The dilatation of the bile ducts on the removal of the gall-bladder, the biliary tension equalizer, the occurrence of hydronephrosis in conditions in which the elasticity of the urinary bladder is impaired. According to Matas in arteriovenous aneurism not only the vein is dilated but the artery also as far back as the heart as a result of the abnormal resistance encountered by the arterial current at the point of anastomosis. Circulatory results of valvular heart disease furnish many illustrations.

5. Rarely but to be mentioned as a possible principle, lesions lessening the recoil absorbing power of at least certain proximal portions of the alimentary tract determine a greater motility distal to it. A non-ulcerative localized tumor of the body of the stomach with intact expulsive antral mechanism will result in divulsion of the pylorus and resulting dilatation of the proximal duodenum and in small intestinal hypermotility because the power to absorb peristaltic shock on the part of the stomach has been impaired through loss of elasticity. The lax pylorus characteristic of gastric ulcer of the pars media is perhaps the result of slight divulsion through similar conditions.

6. It has been assumed that tension within the alimentary tube if not a constant throughout still may be proximally influenced by changes in distal tension. Conditions favoring transmission of pressure are fairly obvious in the small intestine especially in the ileum; very much less so in the colon, particularly in parts filled with heavy fecal matter.

There seems however a factor that makes this quite possible. This factor is the existence of an undescribed slowly progressing peripheral colonic motility about the central fecal column in cylindrical fashion which seems to me to be the essential motility of the colon, certainly of the transverse colon. X-ray plates commonly indicate this peripheral motility which is perhaps largely the resultant of intermittent cecal pressure and allows of direct and immediate contact of on-coming matter with the colonic wall for purposes of absorption, an action much furthered by the haustration of the colon. The haustra act as resistance units to this peripheral current, as stations for delay and deliberate absorption from their contents and prevent the dislocation and progression of the column en masse as occurs in the infrequent great colonic movements suggestively during which haustration is abolished and the parts of the colon concerned become a cylinder. This type of motility results in peripheral stratified accretion to the haustral contents through inspissation to the formation of scybalae. Scybalae are thus largely the product of gradual surface accumulation. This peripheral current probably makes possible an approach to a common intracolonic pressure on account of its comparative fluidity and allows for the proximal transmission of increased distal tension judging by analogy and X-ray evidence. There is as mentioned previously much to suggest that colonic tension may thus be transmitted in part on this peripheral current not only throughout the colon but through the ileocecal valve, under normal conditions during periods when it is open, and under abnormal conditions of increased intracolonic tension to its gradually acquired partial or even complete incompetence with secondary recoil and relative stasis in the small intestine. The ileocecal valve may so be forced and become permanently incompetent in the same way that the cardia is divulsed and rendered incompetent in contracting carcinoma of the stomach to the persistence of a constant oesophageal content.

This conception of tension transmission may help to throw light on various problems. On the functional dyspepsias associated with constipation through secondary small intestinal relative stasis and hypertension, especially in the spastic constipations with their more marked pressure symptoms and indicate why there is such variability in symptoms in different types of constipation. On appendicitis and the curiously beneficial results of surgery in certain cases of chronic appendicitis which cause small intestinal recoil through resistance offered and the lack of improvement in others in which the small intestinal stasis

is due to permanent pericecal changes. It may help to explain the close relationship between constipation and appendicitis through the irritating effects of stasis in the appendix, just as diverticulitis results from stasis and irritation by retained fecal matter in colonic diverticula. We all know what a proportion of persons suffering from spastic constipation are adorned with appendectomy scars. In this connection it is interesting that according to W. J. Mayo approximately one-third of the cases of colonic diverticulitis have had appendectomies, suggesting appendicular irritation as the result of the same colonic hypertension that gave rise to the diverticulosis. The form of the appendix usually suggests the presence of increased intracolonic tension through its outline and direction indicating over-distension and dilatation spectacularly in organic colonic obstruction. In periods of constipation the appendix through its form gives these indications of tension and irritation through increased tenderness which are absent after a thorough defecation.⁴ Through its form the appendix is thus a sort of barometer of intracolonic tension. It sounds fantastical but the appendix may possibly have a tension equalizing function similar to that of the gall-bladder. The well founded surgical rule against the use of purgatives in cases of acute appendicitis illustrates the practical value of an appreciation of the transmission of colonic tension to the appendix. Those of us who have seen castor oil floating in fecal matter among the intestines at an emergency operation have no doubt of the desirability of any new light on the question. It is generally taught that the rupture of the acutely inflamed appendix after a purgative is the result of excited colonic peristalsis. It is primarily so but the actual force that results in the appendicular blow-out is probably applied through the increase in the common intracolonic and appendicular tension.

If true the idea of visceral hypertension, its transmission and results, may resolve certain great problems in gastro-enterology to something of a common relationship. Many cases of constipation, many cases of appendicitis, the formation and points of occurrence of multiple colonic diverticula at points of maximum tension as in the abrupt curves of the pelvic and ileac colons and just proximal to points where

⁴ As an aside it may be noted that the appendix is more tender to pressure when intracolonic tension is increased as in periods of constipation suggesting irritation as the result of such tension. An appendix that is suggestively tender at such a time will generally be much less so after a laxative. The same holds true in the case of a spastic ileac or pelvic colon and in other conditions.

the colon is compressed as by uterine fibroid or other obstruction of gradual causation. The fact that colonic diverticulosis practically only occurs in sthenic and hypersthenic types, except where an obstruction has developed, in whom visceral tonus is inherently great and alimentary motility more rapid suggests that intracolonic hypertension is the essential cause of diverticulosis. Purgative abuse is probably a chief immediate contributory causative factor. Colonic redundancy which seems to me for certain reasons to be chiefly acquired and not congenital may be an expression of somewhat similar conditions of increased intracolonic tension resulting from fecal retention reacting in a colon of different type and of an essentially lower degree of tonus. Constipation and purgative abuse seem here also the primary causative factors. If all this be true or only in part true it points to the tremendous importance of the correction of constipation and especially its prophylaxis in children through better home, school and industrial hygiene, popular education and so on.

Visceral hypertension and recoil may help to explain auto-intoxication through small intestinal stasis, recalling our not entirely satisfactory efforts to adequately account for it on the basis of a pathological absorption from the colon. It may help to explain the contention of the functionally dyspeptic patient that he is full—as he interprets it—of gas, which the X-ray shows is not gas, his coated tongue, his relief on belching or passing flatus through temporary relief of his intra-alimentary hypertension, his distress after inadequate defecation, his improvement on the improvement of his constipation and his insistence on calomel instead of a diet—the guiding principle—the physis of the ages. It may be that in the future we shall attach as much importance to studies of intra-alimentary tension as we now do to blood pressure observations. Certainly its actual determination if possible, perhaps by a modified intestinal tube, would be most interesting. It is probable that intra-alimentary tension would be found to be actually very slight could it be determined and expressed by manometry as suggested by the very moderate degree of pressure necessary to cause a barium enema to retrogress. It is disturbance in relative tensions in different locations that is abnormal and disorganizing.

7. Whenever there is over-rapid small intestinal motility from any source, the small intestinal forms will reflect this indicating over-distension and increased fluidity of the intestinal contents more noticeable in the jejunum. The simplest illustration is that of conditions after a gastro-jejunostomy in which the small intestine chiefly the jejunum is

often obviously over-distended and at operation can be demonstrated to be dilated. The same thing occurs in achylia gastrica in spite of X-ray suggestions of a normal gastric motility and normal pyloric sphincteric action. Frequently the same type of distended loops of small intestine are associated with diarrhea suggesting that this is not altogether colonic as has been supposed.

There are arguments against the idea of a relative small intestinal stasis. It may perhaps be justly assumed that the presence of atypical small intestinal forms lacks the conclusiveness of a time motility pressure determining experiment. It is admitted; yet I must urge the overwhelming and suggestive constancy of such findings as have been mentioned in association with certain conditions. It must answer for the present; there are no observations as to the exact rate of small intestinal motility even under normal dietary conditions, a tremendously difficult problem considering physical type and individual variation as to the rate of alimentary motility in response to the same test in different persons. A most refreshing experience has been that in two instances I have been able to predict obstructive organic lesions of the colon overlooked at the time of examination several years previous from the form of the small intestine in reviewing plates for this article.

The fact that atypical small intestinal forms are seen after appendectomy without persistence of symptoms is interrogating. Yet the impression is that they are less marked; the reaction may be lesser in degree, or there may be a persistence of acquired hypotonicity without hypertension sufficient to cause symptoms.

The most effective argument against the whole idea is that lesser grades of organic small intestinal obstruction are not associated with exactly the same clinical picture as in functional dyspepsia. However, it would be easier to account for this dissimilarity of symptoms as between these conditions on the ground of dissimilar conditions and the probability of a different protective response and individual nervous sensitization than to discount entirely evidence in favor of the conception. There are frequent cases of functional dyspepsia in which the pressure symptoms attributed by the patient to "gas" are marked yet no commensurate atypical small intestinal forms are apparent on the plate; yet there may be an intra-intestinal hypertension without dilatation through the response of increased tonus on the part of the intestinal wall or other protective reactions. Occasionally the same type of small intestinal loops is to be seen in asthenics and debilitated persons, in cases of hernia (though in this latter instance there may be

suggestive resulting symptoms) and after laxatives. Still many sorts of valuable information must be judged in the light of their exceptions. The foregoing emphasizes that the interpretation of atypical small intestinal forms is decidedly a matter of judgment after the consideration of various influencing factors.

It may be objected that in this day of complicated physiological studies of alimentary secretions, endocrine disturbances, neuromuscular reactions and so on that so simple a mechanical theory is inadequate and improbable. It may be so, yet our most effective knowledge of alimentary disturbances has been gained through an understanding of motility and its abnormalities. Often the directly active forces in the causation of disease are comparatively simple.

I can think of no argument that would discredit the idea of a peripheral colonic motility. I can demonstrate it in a thousand plates—any colon plate taken at a suitable time after a fed test. How is it that the head of the barium column seems to slowly and faintly progress across the transverse colon without dislocating the contents ahead. Instead barium first appears distally as a thin film outlining the already filled colon—not mixing with its contents but surrounding them. Not very infrequently barium will be seen to have reached the rectum by the time the stomach is empty without a defecation having occurred. It must have passed peripherally. The haustra do not give evidence of having considerably changed. A barium enema given with the colon filled with feces retrogresses peripherally. Often constipated persons taking mineral oil complain of passing it alone without a bowel movement having occurred. There is reason to think that this peripheral migration at times at least occurs intermittently possibly as a result of periodic expulsive activity of cecum or ascending colon. There is too not in original evidence to suggest that it may progress without proximal propulsion; the median transverse colon alone being sometimes first faintly outlined with the cecum the only other portion of the colon filled. The relatively long delay at the hepatic flexure suggests some sort of preparatory function in the proximal colon. The great colonic movement is but a general collection, clearing the stage for a new setting of the same act.

DISCUSSION

DR. J. W. DRAPER, New York: I would like to ask Dr. Mills—I did not understand whether he offered any explanation for the recoil and to call the attention of the Society to the work done by Dr. Howard Barber on neuromuscular control. As I recall it, he found that he could produce dilatation of the pylorus by a gradual and incomplete obstruction at the terminal ileum whereas if the obstruction were complete—in experimental animals, of course—the pylorus closed at once. It seems to me a part of this explanation might be due to neuromuscular control as well as to mechanical recoil which I assume Dr. Mills will confirm. The extensive physiological and biochemical reactions of the alimentary canal must not be lost sight of because of mechanical considerations which are of equal importance.

DR. GEORGE B. EUSTERMAN, Rochester, Minnesota: I want to subscribe to one observation in which I uphold Dr. Mills. In the last three months I have seen 3 cases of duodenal cancer in the second and third portions. Primary cancer of the small bowel is exceedingly rare; and the clinical features were those of pyloric obstruction. The patients were elderly and had all the symptoms of cancer of the stomach. Roentgenological examination and surgical exploration revealed carcinoma of the second and third portions of the duodenum. The point I want to make is that we saw the same dilatation of the stomach, the decompensation of the pyloric mechanism as shown so beautifully in these slides.

I think this is a new and fairly complete study not only of the functional but of the organic derangements of the small bowel, of which we have seen little in this country, and I want to congratulate Dr. Mills on this important study.

DR. HORACE W. SOPER, St. Louis: The standardization of gastrointestinal motility in health is necessary in order to formulate correct notions in regard to the treatment of motility disturbances. Alvarez's concept of a gradient of peristalsis beginning at the mouth and ending at the anus must be kept in mind. Concurrently with the ordinary peristaltic rhythm must be presupposed rhythmical biochemical processes. Interruption or delay in the ordinary sequence of events in the gastrointestinal tract perhaps originates the functional disorders to which Dr. Mills has referred, particularly the dyspepsias and the auto-intoxication syndrome, et cetera. Evidence is accumulating to the effect that conditions in the lower colon may produce a "block" that recoils throughout the entire gastrointestinal tract. It is obvious that restoration of physiologic colonic motility in these cases forms the basis of rational therapy.

DR. B. W. SIPPY, Chicago: It may be worth while to mention 3 cases, 2 of carcinoma, 1 in the lower portion of the duodenum and 1 in the upper portion of the jejunum and in those cases the obstruction was not at all tight, but there would be vomiting and gastrointestinal disturbances. The striking feature in these cases was that there were peristaltic waves in both cases in the stomach, very definite and seen in the office. They were apparently pyloric obstruction cases. They had slight retention and vomiting, one of extreme grade producing dehydration. Whether the sphincter was divulsed we do not know because the obstruction lower down produced an increased work on the stomach wall and hypertrophy. Another

remarkable case was obstruction reflected up the abdominal wall in a man of large size which occurred in 1913—a case of carcinoma in the splenic flexure of the colon with definite peristaltic waves from left to right, lifting up the stomach wall. Was that divulsion? Was that reflex pyloric spasm? The case is still alive, and nothing found at the pylorus to cause the obstruction.

DR. R. WALTER MILLS, St. Louis (closing): I took so much time inadvertently that I do not want to say any more except to answer Dr. Draper's question. My own explanation is that the delayed gastric motility is probably on the basis of mechanics. The majority of our advances have been made by the understanding of mechanical things in the gastro-intestinal tract and impairments of motility. Distal physical abnormalities making for resistance seem proximally reflected throughout the alimentary tract. There is evidence that suggests that the same thing occurs to a lesser degree in functional disturbances as in marked constipation. It may be that proximal intra-alimentary tension throughout the alimentary tract is increased in constipation, the same type of recoil that occurs in colonic obstruction only to a lesser degree.

GASTROINTESTINAL INFECTION IN RELATION TO INFECTION OF THE LIVER AND BILE PASSAGES (A CONTINUATION)

CHARLES G. STOCKTON

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RÉSUMÉ OF FORMER REPORT

In 1916 the patient first appeared, suffering from debility, hypochlorhydria, lowered nutrition; there were no symptoms related to liver or intestine. She was discharged eight weeks later, showing general improvement, and was in good health until the spring of 1919, when there developed intractable diarrhea. She returned to Buffalo in September, 1919, with gastroenterocolitis, of greatest intensity in the small intestine, with gas bacilli and streptococci abundant. The stomach showed atonic dilatation, achylia, pus cells, red blood cells and an excess of mucus. In November, 1919, the diarrhea was controlled, gastric secretion reappeared, and the patient was discharged, taking a smooth diet. Improvement continued for a month, with a gain in weight of 14 pounds, but the patient ate too freely and became for the first time jaundiced. On December 24, three weeks later, she came again to Buffalo. There was complete associated jaundice, with acholic stools. A study of the stomach and duodenal contents indicated severe duodenitis. There was a recurrence of diarrhea. The liver was enlarged and slightly tender to pressure, but there was no pain.

Conclusion: Biliary obstruction from swelling at ampulla of Vater.

There was slight elevation of temperature and a leucocyte count of 6100. Duodenal lavage was practiced with benefit. The jaundice diminished, became intermittent with occasional rigors, followed by fever and renewed jaundice with leucocytosis. The clinical picture corresponded with the old conceptions of angiocholitis. The intestine, including the colon, showed atony and catarrhal inflammation. Under deep duodenal feeding, duodenal lavage and colonic irrigations the patient improved. In May, 1920, recovery seemed possible, as stated at our last meeting.

HISTORY OF THE CASE AS DEVELOPED SUBSEQUENT TO THE REPORT
MADE AT THE LAST MEETING OF THE ASSOCIATION

The patient had almost invariably a good appetite. At times there was slight gastric secretion (hypochlorhydria), at other times secretion was absent, with evidence of a low-grade gastritis. Intermittently the stools showed bile coloring matter and bile salts, not always associated. She was not studied as to the presence of hemoconias. In the duodenal contents pancreatic ferments were very deficient. There was feeble amylitic enzyme, still feebler proteolytic enzyme, and usually absence of lipase action. Always there was mucus in excess, occurring often in shreds, containing numerous pus cells, at times many degenerated red blood cells.

It was evident that there was an open passage through the bile ducts, but nevertheless infection coming through the biliary channels. This was proved by the use of the duodenal tube after irrigation of the stomach and duodenum. It was also evident that there was a very defective digestive power in the duodenum, as a result of the disordered pancreas and the duodenitis. At this time the suggestion was made by Dr. Rose Donk, who was assisting on the case, that the transfusion of normal duodenal contents from a healthy donor might provide the patient with needed digestive ferments and help her to gain in nutrition. This treatment was carried out by Dr. Donk under my observation during a period of two weeks. The healthy donor while fasting, having had passed the duodenal tube and having had the secretions stimulated by small quantities of hot water, gave out from 60 to 200 cc. of duodenal contents, which was immediately introduced through a tube into the duodenum of the patient. The result of this treatment was published by Dr. Donk in the *Journal of the American Medical Association* of November 13, 1920, under the title "Transfusion of duodenal contents." The work was interesting and unquestionably the patient received temporary benefit from the measure. I am convinced that this suggestion made by Dr. Donk will prove to be of some practical importance in selected cases.

Intestinal perfusion was also practiced at other times with apparent benefit. A freer flow of bile was promoted by irrigation with magnesium sulphate solution as suggested by Meltzer. The diarrhea never recurred with its former intensity, yet there was a continued predisposition to looseness requiring attention and at times special medication. The sigmoidoscope revealed a catarrhal colitis, but no

bleeding points. The patient in February had a definite intestinal hemorrhage unexplained in origin.

Medical and surgical consultants leaned to the opinion that there was more trouble in the gall-bladder than had been hitherto believed. It was suggested that we were dealing with a chronic cholecystitis with calculi. There was no evidence of this, however, in the radiograms which were shown and discussed at our last meeting. To my mind it seemed clear that the trouble was not from the gall-bladder, but that we had, following the blocking at the papilla in the beginning of the jaundice, an ascending infection which reached the liver and probably the pancreas.

During May the case was at a standstill, with an occasional discouraging relapse; that is, chills, fever, and leucocytosis, the attack lasting two or three days; then the jaundice would fade, but it never disappeared. It was decided finally that there should be made a cholecystostomy, with the hope that by removing a cholecystitis, the infection passing into the intestine would be eliminated and that the patient might be benefited. Also it would settle the question as to calculi.

The operation was made under gas and ether anesthesia, which was preceded by a transfusion of 750 cc. of blood from a well-typed donor. The transfusion was intended not only to strengthen the patient, but to increase the coagulability of the blood, which had been found to be fourteen minutes plus. Following the transfusion Dr. James A. MacLeod operated upon the patient, removing the appendix, which showed chronic inflammation, and performing cholecystostomy. It was decided to do little exploring, so that the shock might be at the minimum. However, it was found that there was no evidence of tumor about the stomach or duodenum; the pancreas was unusually firm on palpation, the gall-bladder was not distended but was rather pale, and contained no calculi, but a small amount of rather dark bile of increased consistency. The liver was apparently moderately enlarged, was pale yellow in color, rather firm upon palpation, with the surface irregular as seen in cirrhosis. The common duct was not explored.

The patient endured the operation remarkably well, and seemed to be in better condition after it than before, doubtless from the transfusion. The amount of bile drainage was small, and we felt that little was directly gained by the operation. For some days, however, the patient did well, when there ensued another, and this time severe

intestinal hemorrhage, and transfusion seemed necessary to save life; 500 cc. of blood were therefore introduced into a vein. The blood was taken from a new donor. There was no agglutination shown on typing, but subsequently it was found that the patient's serum hemolyzed the donor's corpuscles. There followed great prostration with unconsciousness. In the state of depression amounting almost to shock which followed the second transfusion with blood, there appeared in the urine a very large amount of urobilin. Previously it never had appeared in the urine, and after that event it never disappeared. It is an interesting question as to what effect this transfusion may have had upon the liver to hasten its degeneration, in its already crippled and infected state. There is of course the possibility of coincidence, but the clinical fact remains striking. For a few days it looked as though the patient would succumb from hemolysis and proteid poisoning. However, she rallied and matters progressed favorably for a few days, although there continued to be marked urobilinuria. At this time drainage of bile was insignificant, and it occurred to me that benefit might follow irrigation of the gall-bladder through the drainage tube, with a magnesium sulphate solution of 25 per cent. This was practiced with the result that the drainage of dark colored bile was much increased. There was considerable diminution of the jaundice, which had deepened since the operation. I think that real but transient improvement followed this irrigation of the gall-bladder with a magnesium sulphate solution. This was carried out for a month, the patient making slow improvement. The evidences of infection were less conspicuous, that is to say there was absence of chills, but slight temperature. Under the treatment the liver shrank in size and it was difficult to keep a drainage tube in place for purposes of irrigation. Finally irrigation became impossible, the wound healed, and the patient was sent to her home.

She made the journey of 150 miles with little difficulty, and continued with but little change in her condition for about a month, when she somewhat suddenly went into a collapse and died.

Dr. William F. Jacobs, pathologist, accompanied me to her home, and there was made a careful but incomplete autopsy, limited to examination of abdominal viscera. The results of this postmortem study were interesting. The stomach showed dilatation, with gastritis. From the gross appearance the mucous tissues of the duodenum were infiltrated, swollen, intensely red and somewhat softened. This catarrhal state of the intestine was observed throughout the

gut, being less evident in the colon than in the small intestine, and more marked in the duodenum than elsewhere. There were no adhesions from the appendectomy. There were the usual adhesions at the sight of the cholecystostomy. From microscopic sections the tunics of the stomach and intestine showed less inflammatory change than would have been anticipated from their appearance, yet on microscopic section marked duodenitis was demonstrated. The gall-bladder was contracted, but showed no growth on culture. The

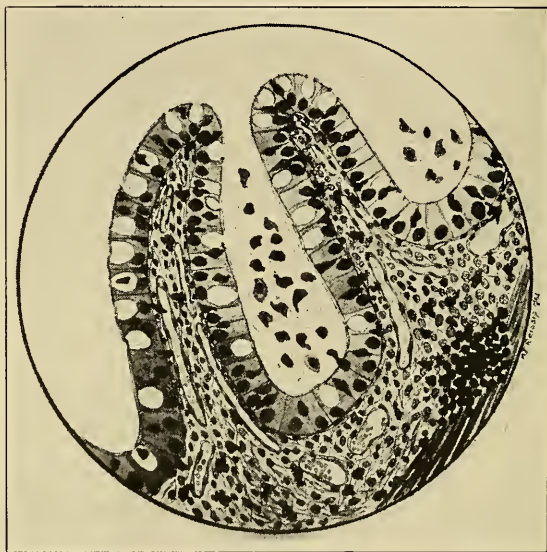


FIG. 1. QUITE LOW POWER PHOTOMICROGRAPH OF LIVER: AN AREA OF WELL STAINED LIVER TISSUE SHADING INTO UNSTAINED AND NECROTIC TISSUE; ALSO CELLULAR FIBROUS TISSUE WITH BILE DUCTS

biliary passages, including the common duct, cystic duct and hepatic duct, were healthy. There was no evidence of calculus past or present, nor was there evidence of past cholangitis.

The striking and interesting features of the case were found in the structures of the liver itself. This organ had shrunk to perhaps two-thirds its normal volume, which it will be recalled was large during the six months preceding the operation and also at that time. It was yellowish, fawn-colored, with small irregularities of surface such as one sees in hepatic cirrhosis. On incision of the liver, in all parts of

the organ, there were found countless areas of necrosis, rather dry in character, containing debris. The tissues presented the picture of minute areas of hepatitis, in which the biliary passages escaped except at their origin, as occurs in biliary cirrhosis. There was marked ingrowth of connective tissue containing many new formed bile ducts. The pancreas showed but slight interstitial change, no evidence of actual infection.

From a strictly postmortem point of view it might seem that the process had begun in the liver and that the bile had led to infection of

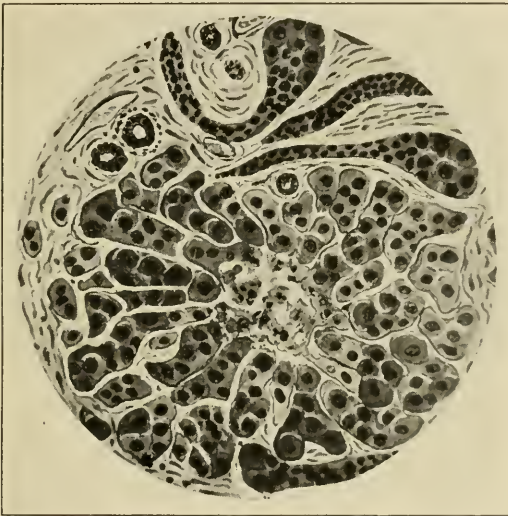


FIG. 2. HIGH POWER DIAGRAMMATIC SKETCH OF PART OF A LIVER LOBULE, WITH SMALL CENTRAL AREA OF NECROSIS, AND NEW FORMING BILE DUCTS AT THE EDGE

the intestinal tract. Such a conclusion does not correspond with the history of the case. It will be recalled that the patient suffered primarily from gastritis and failing gastric function, and three years later from enteritis, and was subsequently never free from these conditions. There was no jaundice preceding the last eight months of life. It is my own judgment (and I think the morbid structures support this view) that the disease was primarily a gastritis, later an intense duodenitis; that there was from swelling of the duodenal mucosa a blocking at the papilla, which caused the first attack of

jaundice. Meantime infection had been carried to the liver through the portal system, and thus there was set up a hepatitis with descending inflammation, and not one that ascended through the biliary tract, as I had naturally inferred. I feel that this statement is worthy of repetition and emphasis, for the reason that this case seems to illustrate the growing belief that jaundice is more often the result of an infective or toxic hepatitis, with the infection descending, than an ascending

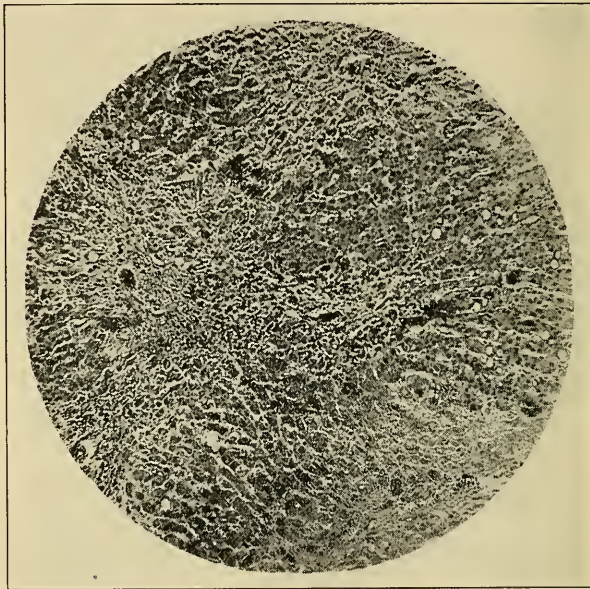


FIG. 3. HIGH POWER SKETCH OF INTESTINE WITH TWO VILLI: NUMEROUS GOBLET CELLS AMONG THE SURFACE EPITHELIAL CELLS, LEUCOCYTES FREE BETWEEN THE VILLI AND MIGRATING THROUGH THE EPITHELIUM; DILATED CAPILLARIES, CELL COLLECTION IN THE SUBMUCOSA, ALL INDICATING SUBACUTE ENTERITIS

infection; that is to say, the infection reaches the liver through the portal system, and the obstruction to the outflowing bile occurs in and about the lobules and possibly at the beginning biliary passages. This is not to deny the well known fact that jaundice often arises from obstruction at the common duct or the hepatic duct, and this obstruction may of course be inflammatory. Except in the instance of calculi causing actual obstruction at the junction of the cystic and common ducts or in the ampulla, jaundice is probably rather rare from simple

angiocholitis of ascending nature. In another paper to be read before the Section of Gastroenterology of the American Medical Association, this phase of the matter is gone into at length.

There are the following outstanding features to the history of the case:

1. The relationship that may exist between hepatitis, with necrotic areas, later replaced by interstitial ingrowth on the one hand, and on the other hand persistent gastroenterocolitis, in some regions intense.

2. With this pathology, nevertheless, there was escape from involvement or inflammation of the chief bile channels and the gall-bladder, as shown during life by operation and later by postmortem.

3. The illustration of possibly beneficial results from a novel method of treatment, that of transfusion of the normal duodenal content of a healthy donor into the functionless duodenum of a patient; also the value of intestinal perfusion.

4. The remarkable effect in stimulating the flow of bile from a badly diseased liver by direct irrigation of the gall-bladder with a magnesium sulphate solution. This also is, so far as I know, a novel measure of treatment, and is interesting to compare with the method of stimulating the outflow of bile as described by Vincent Lyon.

DISCUSSION

DR. JOHN A. LICHTY, Pittsburgh: I discussed this paper last year when Dr. Stockton presented it to this Association and I came very near criticizing him for not having operated on his patient before that time. I now have a very different view of the case and would like to ask Dr. Stockton whether he feels that the operation, performed at the time it was, in any way hastened the death of his patient? Whatever answer the Doctor may give, I bow to his wisdom in this case.

Another point: there seems to be a striking parallel between infection at the papilla of Vater, its frequency, and the infrequency of such an infection as Dr. Stockton's case represents, where there is infection at the terminal radicles of the biliary tract. May we not have the same parallelism in malignancy of the biliary tract? The frequency of malignancy of the papilla is well known compared with carcinoma anywhere else along the biliary tract, excluding the gall-bladder, whereas the infrequency of malignancy in the terminal radicles of the biliary tract, in certain cases of primary carcinoma, is very rare. There seems, therefore, to be a peculiar similarity between the chronic infections of the biliary tract and the malignant involvement of the biliary tract, considering the proximal and the distal ends.

The malignant side of this is well demonstrated in a case which I shall report in my paper today.

DR. B. B. CROHN, New York: This case has interested me. About three years ago I saw a woman who in complete health developed ——— at that time I was struck by this case because I seemed struck by the fact that she had a carcinomatous lesion at the papilla of Vater. She was operated on, and there was no obstruction found at the common duct or in any part of the biliary tract. Probes were passed through. The woman went through the operation and had hemorrhage and a tube passed through the bile duct brought no bile at all. She went for ten days without passing more than 10 ounces of bile all of which came from the intestinal tube. At the autopsy there was no lesion found except a small liver, which liver, on histological section, showed some degeneration of the cells. The case was puzzling at the time. I did not know what to make of it. A few weeks ago I saw a same identical case in New York in a woman who had salvarsan treatment in New York for lues. This woman was operated on for supposed obstruction at the common bile duct supposed to be due to stone, and no obstruction was found. This woman became toxic, died after the operation, not with hemorrhages but with symptoms of acute yellow atrophy of the liver, and again at autopsy a small liver was found with some degeneration of the cells. The pathologist who reported the case, reported it as a case of acute catarrhal jaundice which I took exception to.

A third case was operated on and nothing found, but some adhesions. I saw 2 cases and found a third, and in discussing with some men I found that they had in all 5 cases of the clinical picture one in which there was suppression of bile formation corresponding to a case in the kidney called nephrosis. I do not know what the analogous word would be in the liver, but a degeneration of the secreting part of the liver leading to complete suppression of bile and jaundice goes on to a toxic picture in which death takes place by cholemia or hemorrhage.

I feel that we are dealing with a new clinical picture not like acute yellow atrophy. What the histological picture is I do not know. I do not think it is an infectious disease, but a metabolic disease.

DR. JULIUS FRIEDENWALD, Baltimore: I should like to report a case in which there was an apparent obstruction to the common duct due to some external cause and which was of considerable interest. The patient was a man forty years of age who presented himself for examination a few weeks ago.

We found him markedly jaundiced and as he had lost some flesh and had comparatively but little pain, the diagnosis of cancer of the pancreas seemed most probable. He was apparently in sufficiently good health to warrant an exploratory incision and Dr. Finney was about to operate on him one morning when just preceding the time of the operation he suddenly collapsed, evidently from hemorrhage and was unable to undergo the surgical procedure. Another fainting spell of a similar character followed notwithstanding the fact that a transfusion had been given him.

At the autopsy the abdomen was found filled with blood and many clots and the common duct was obstructed by an aneurysm of the hepatic artery which had ruptured and had caused the patient's death; it was evident that the weight of the mass on the common duct had caused the jaundice.

DR. B. B. VINCENT LYON, Philadelphia: I would like to ask about the bacteriological studies during life, and the second question I would like to ask, how many duodenal *infusion drainages* were given during life and magnesium sulphate introduced through the gall-bladder; third, I want to speak about a case which came to my mind emphasized by what Dr. Hemmeter spoke of, about hemolytic jaundice. The absence of the enlargement of the spleen was against that type. We have under observation at present a case that will be reported this week, a very interesting case of hemolytic jaundice which we have had under observation for eight months and has been of a total duration of three years with an enlarged liver and very much enlarged spleen and presenting waving of the abdomen with positive cultures of hemolytic streptococci which are delivered from the bile which under treatment has made one of the most remarkable restorations. Some of the men in this room have seen this case. Dr. Krumhaar of Philadelphia has seen him, and the motility tests have pointed to hemolytic jaundice. Now the transition in that man's condition after eight months is in every respect extraordinary, and I hope to have a chance later on to go into it in detail. It is particularly in the bacteriology and the number of drainages prior to operation that I was interested in Dr. Stockton's paper, and besides that whether the hepatic gall tract condition did not precede the gastroenterocolitis which may be the remarkable picture from a symptomatic standpoint and may be masking the primary incidence in the liver and gall-bladder.

DR. JOHN C. HEMMETER, Baltimore: Before I discuss this address I would like to ask Dr. Stockton about the histology of the spleen.

DR. STOCKTON: Apparently there was nothing unusual about the spleen. There was no enlargement of the spleen.

DR. HEMMETER: This shows what can be done when a case gets into the hands of a master like Dr. Stockton who can follow it up. I wish to emphasize that the jaundice may be a hemolytic jaundice in spite of all the changes in the liver. The microscopic pictures of the histology of the liver suggested one case that I saw in a girl (Dr. Hemmeter illustrating by drawing on board). We will say that this is a bile duct and the lymph spaces outside here. Now in the walls of the capillaries are elongated cells which are called Kupffer stellate cells, after their discoverer. They are multiplied in some types of cirrhosis. The cell is an apparatus for the deglobulation of the red blood corpuscles, and they are much increased in number and in size in this form of hepatitis. They are also organs of defense placed at the entry into the liver of the great amount of blood that comes from the vast absorptive surface, the gastrointestinal canal.

I was interested in this valuable paper, but the second picture emphasized to me that in spite of all the evidence of a purely hepatic case there was an element of hemolytic jaundice. The Kupffer cells at times become the victims of their marked phagocytic power and as a result they break down and desquamate from the capillary lining and form pigment thrombi. Such desquamated hepatic Kupffer cells may become the focus of inflammation and create a necrobiosis in their immediate environment producing a circumscribed hepatitis.

DR. CHARLES STOCKTON, Buffalo: Some of the questions which have been asked will be better answered in the paper which I hope to read before the Section on Gastro-Enterology and Proctology of the American Medical Association, dealing more fully with the hepatic side of these cases. In the case reported I dare say that there was a slight degree of hemolysis. However, there was proof that the jaundice was of liver origin; there was absence of bile salts in the stools at times, and other times, also, there was the absence of the coloring matter. The case illustrated both associated and dissociated jaundice. The serum of the blood was examined. There was no enlargement of the spleen. The conspicuous changes were in the liver.

Dr. Lichty asked about the result of operation. I do not think the operation did the patient any harm, and I doubt if it did any good. It was interesting and instructive to us. It did the physician good. It showed that there were no gall-stones, no cholecystitis and no cholangitis; it possibly helped the patient by enabling us to use the gall-bladder irrigations which I will speak of later.

Dr. Bettmann asked about the bacteriological study. The predominant organism was the gas bacillus, very active in the intestine, in the colon and at times in the small intestine, particularly in the duodenum. Also we found a hemolytic streptococcus and the colon bacillus. The singular fact was that while this infection seemed to be the cause of the liver infection, the bile which was taken at autopsy was sterile. The bile which was removed at the time of the operation was sterile. It was dark, cloudy and viscid. It came from a liver that showed necrosis, but we failed to get growths from our cultures.

As to the number of magnesium sulphate treatments prior to the operation—they were given repeatedly, on several occasions. We secured free flow of bile following the magnesium sulphate infusions.

The striking thing about the case to my mind was the remarkable flow of bile that occurred from the direct irrigation of the gall-bladder through the tube with magnesium sulphate solution. There was more bile from that than from anything we did in the case. We were very careful not to have back pressure in the bile passages and we secured a perfectly normal return without pressure; and following that the bile began to flow and flow freely so long as we kept it up, but through the repair process irrigation became impracticable. The liver became so small it was difficult to reach the gall-bladder under the ribs.

The question, did the disease of the liver precede the disease of the intestine or vice versa, I think very live and important. A good deal of discussion is going on abroad as to the relation of the digestive tract to diseases of the liver and bile passages, and it seems to me to be of the utmost importance. I do not think it is altogether infection, but also intoxication. The effect of one enhances the activity of the other. That is the trend of recent thought; it would account for acute yellow atrophy and for cirrhosis, not by one agency, for instance, alcohol, but by a variety of toxic influences, including sensitization or proteid poisoning, reaching the liver and preparing the ground for infection. There is more than one factor that produces necrosis and cirrhosis, which this case illustrated. It suggests the etiology of those tragic cases of necrosis which we have been calling acute yellow atrophy for lack of a better name to give them.

DR. HEMMETER: I should like to call attention to the fact that the treatment of intestinal putrefaction by bismuth subnitrate is dangerous if continued too long; for, if the intestine contains sulphuretted hydrogen the subnitrate is converted into a nitrite and all nitrites are poison. Basic bismuth salts when they come in contact with fresh wounds for instance intestinal ulcers, are rendered soluble without exception, thus a severe bismuth poisoning may be the result of the treatment of intestinal ulcers with basic insoluble bismuth salts. It is an error to speak of any bismuth combination as absolutely harmless.

THE RECTO-SIGMOID APPARATUS: ANATOMY, PHYSIOLOGY, PATHOLOGY

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ANATOMICAL CONSIDERATIONS

The iliac colon extends from the crest of the ilium to the inner border of the left psoas muscle. It is the only portion of the lower colon that is always accessible to palpation. The pelvic colon forms a freely movable loop, varying in length from 5 to 33 inches, the average length being about 17 inches. It has no constant position, but in its most typical arrangement passes from the termination of the iliac colon at the inner border of the left psoas muscle, loops to the right, and ends in front of the third sacral vertebra, where its junction with the rectum forms the pelvi-rectal flexure. The rectum is between 4 and 5 inches in length and lies in contact with the sacrum and coccyx. At its termination the rectum bends slightly backwards and merges into the anal canal. The anal canal, about 1 to $1\frac{1}{4}$ inches in length, is directed downwards and backwards forming almost a right angle with the rectum. It forms a narrow canal with longitudinal folds of mucous membrane, surrounded by the muscle fibers that form the external and internal sphincter apparatus.

It is impossible to enter into a description of the diseases that involve the lower intestinal tract without some consideration of the topography of the entire colon. The usual description above applies very well to the average normal subject as the organs appear at autopsy. In the living individual, the anatomical relationships are not constant, but vary with the structure or bodily habitus of the individual.

Mills, in his work on habitus, has demonstrated that the visceral contents of the abdominal cavity conform to certain definitely recognizable anatomic types. The most striking variation is shown in the differences in the position and form of the stomach. Mention may be made here of the long narrow fishhook-formed stomach of the asthenic, extending to the pelvis, in contradistinction to the almost transverse high stomach of the hypersthenic.

The colon also shows very marked variations corresponding to the bodily habitus of the individual. In the hypersthenic, the sigmoid loop or pelvic colon, is high above the pelvic cavity and really presents but one curve almost circular in character. In the sthenic, the loop is more markedly S-shaped and is contained partly in the pelvis. In the asthenic, a portion of the transverse colon and the pelvic colon are massed together in the pelvic cavity. In each instance, the position assumed by the colon corresponds to its particular anatomic type and is not to be considered as pathological. Therefore, from a clinical standpoint, the consideration of the form and position of the lower colon presents, *a priori*, a very pertinent question, viz., does the colon conform to the bodily habitus, or is there a variation from the individual's anatomic type? For example: the pelvic colon of the asthenic may be pushed out of the pelvis by a tumor mass or the hypersthenic colon may be tied down in the pelvic cavity by inflammatory processes.

The rectum, also, while immovably fixed, shows certain variations corresponding to habitus. In the asthenic type, the anal canal is short, located near the coccyx, and the protoscope enters at once into a large capacious ampulla. In the hypersthenic individual, the anal canal is much longer, situated further from the lower spine, and protoscopy reveals a relatively much smaller ampulla. In many hypersthenic individuals I found, by actual protoscopic measurement (the patients in the knee-shoulder position), that the anal canal was from 2 to $2\frac{1}{2}$ inches in length, while that of the asthenics varied from 1 to $1\frac{1}{2}$ inches in length.

The variation in form, observable in the different anatomic types, is not more striking than the differences exhibited in function. In this connection, one may mention the evident tonicities of the colon in the hypersthenic as compared with the extreme atony of the asthenic colon. The rate of motility is high in the hypersthenic, low in the asthenic, intermediate in the sthenic. It may be physiological for the hypersthenic to defecate two or three times daily, while in the asthenic, the rate may be normally so slow as to permit an evacuation but once in two days. The intestinal tube of the sthenic and hypersthenic is well adapted to the high energy requirements of individuals exhibiting this structural type. On the contrary, the intestinal tube of the asthenic with its atonic character, low position and slow rate of motility, places the asthenic individual at a disadvantage in the machinery required for the production of bodily energy.

A predilection for the development of certain pathological conditions may be associated with habitus, e.g. The asthenic is notably pre-

disposed to colonic stasis and more frequently presents the syndrome which is usually termed "autointoxication." Moreover, the pelvic colon, from its low position, is more likely to become involved in pelvic inflammatory processes. On the other hand, the condition known as diverticulosis occurs more frequently in hypersthénics and sthénics.

William J. Mayo has made a very careful study of the recto-sigmoid apparatus. He has shown that it consists "of $3\frac{1}{2}$ inches of the intestinal tract, which includes the terminal 2 inches of the sigmoid and the proximal $1\frac{1}{2}$ inches of the rectum." It is the narrowest part of the large intestine and is more often the location of pathologic processes than any part of the gastrointestinal tract excepting the stomach and duodenum. Mayo's study is based upon dissections in 46 cadavers. The terminal sigmoid contracture was found in 80 per cent of cases examined. Mayo has shown that the recto-sigmoid apparatus is controlled by the pelvic plexus of nerves which is made up of a variable number of sympathetic ganglia joined from above by spinal nerves from the lumbar region and from below by the spinal nerves from the sacral region.

Langley and others have shown that nerves derived through the hypogastric plexus are inhibitory in character, while those from the spinal and sacral nerves produce contracture of the muscle fibers of the intestine upon stimulation.

Keith has shown that the smooth muscle fibers in this region have the power of originating contraction and that impulses are collected in certain neuromuscular nodes and correlated.

Mayo and Arthur Hurst both are of the opinion that the failure of coördination in early life results in the so-called idiopathic dilatation of the colon or Hirschsprung's disease. This disease is, therefore, according to Mayo, similar in origin to cardiospasm at the cardiac orifice and ileocecal valve stasis. Hurst has suggested the name of pelvi-rectal achalsia instead of Hirschsprung's disease. According to Hurst the active relaxation of the circular muscle fibers at the pelvi-rectal juncture fails to occur and a spasm is originated, which leads to partial obstruction with consequent dilatation and hypertrophy of the pelvic colon. The colon, when once dilated, produces a kink by overhanging the undilated portion below, thus producing increased difficulty in defecation, progressive accumulation of fecal matter and progressive dilatation and hypertrophy of the muscle fibers of the colon, finally resulting in broken compensation with the loss of peristaltic power.

PHYSIOLOGY

Mayo's anatomical studies have led him to the conclusion that the "recto-sigmoid apparatus is a definite mechanism, which retards the fecal current and prevents continuous progress of the intestinal contents into the rectum." Hurst, who examined a large number of young adults, comes to the same conclusion; he further states that normally the rectum does not contain fecal matter, except during the act of defecation. At other times the fecal column is prevented from entering the rectum by the tonicity of the recto sigmoid apparatus.

The studies of Hurst, Holzkecht, Barclay, Case and others disclose that the colon is emptied by a series of mass movements. When the fecal column which has been held up at the recto-pelvic juncture, enters the rectum the desire to defecate is provoked. As Hurst has shown this desire is not due to stimulation of sensory nerves, inasmuch as they are absent in the rectum except in the mucosa of the anal canal. The reflex is established by means of the "muscle sense" of the distended rectum. The first mass movement empties the rectum and part of the pelvic colon. Secondary mass movements occur and continue until, under normal conditions, the entire large intestine below the splenic flexure is completely emptied.

Hurst has demonstrated that about thirty-three hours' time is required for a meal to be entirely evacuated from the gastro-intestinal tract. Food taken nine hours before the act of defecation should reach the splenic flexure and part of it appear in the feces. These figures represent the time required for the average healthy individual at active muscular work. Modifications must of course be made for the asthenic type who habitually have a slower rate of colonic motility as well as the hypersthenic whose motility is higher than the average individual, as pointed out by Mills in his work on *Habitus*.

While the x-ray is the best means to determine colonic motility simpler tests are available, e.g., a 5-grain carmin capsule or 2 charcoal tablets given with the evening meal should appear (trace at least) in the feces evacuated the following morning. The second morning the entire stool should be colored by the carmin or charcoal. On the third morning there should be no trace of the coloring matter in the feces.

In corroboration of the work of Mayo and Hurst I have examined a large number of patients, both normal and abnormal, by means of the sigmoidoscope and have made the following observations:

1. After normal defecation in the morning the rectum contains either no fecal matter or only slight traces adhering to the mucosa.

2. The normal recto-sigmoid apparatus as viewed through the sigmoidoscope includes from 2 to 3 inches of the bowel and it can be seen to alternately contract and dilate synchronous with respiration.

3. Normal cases present considerable variation in the tonicity of the contracture. It is always possible to pass a $\frac{5}{8}$ inch caliber tube through it.

4. Normal cases examined in the morning prior to the act of defecation reveal the fact that the fecal column is above or just engaging the recto-sigmoid area.

5. The formation of the feces probably occurs in the iliac colon. This is particularly true of the fragmentary form of constipation in which small, hard, round masses appear in the feces.

PATHOLOGY

Mayo has pointed out that in an investigation of the last 100 specimens of cancer of the rectum and recto-sigmoid removed consecutively at St. Mary's Hospital, it was found that 63 per cent of the growths involves the recto-sigmoid, 30 per cent the rectum only and 7 per cent the anal canal.

As I have shown in previous communications polypi are frequently found at the recto-pelvic angle, also that various forms of pus infections often occur; furthermore that spasms or hypertonic contractures of the apparatus are a frequent cause of obstinate constipation, a condition which I have described as sigmoidospasm. I have further demonstrated that a solution of magnesium sulphate applied directly to the contracted area will bring about relaxation of the contracture; if this treatment be continued for a period of weeks or months it will result ultimately in the correction of the spasm and restoration of colonic function. The majority of the cases of sigmoidospasm are associated with a contracture of the iliac colon; however, they may exist independently of each other. The iliac colon is of extreme interest; it is always palpable; under normal conditions it can be made to contract under the palpating fingers as a rather firm finger-like cord. The contracture will, however, not be persistent, but will relax from time to time. In atony of the iliac colon no such contracture can be elicited by palpation. In spasm of the iliac colon we find the presence of a finger-like cord which cannot be made to relax and which is often

tender to pressure. The iliac colon can be reached by injecting the magnesium sulphate solution by means of the sigmoidoscope and a soft rubber tube, with the patient in the knee-chest posture.

Recently we have been working with atonic conditions of the recto-sigmoid apparatus and iliac colon. When magnesium sulphate is taken into the stomach it is partly converted into sodium sulphate and magnesium carbonate, substances which increase the contractile phase of peristalsis, according to Meltzer. The remaining unconverted portion of magnesium sulphate stimulates the inhibitory or relaxing phase of peristalsis, thus producing the well known rush movement of a dose of Epsom salts. Meltzer's definition of tonus is as follows: "The resultant effect of the antagonistic action may be manifest at the same place and at the same time. This is tonus. The degree of character of the tonus depends on the preponderance of one or the other factor."

Goldschmidt and Dayton have shown that the colonic wall is impervious to the passage of magnesium sulphate or sodium sulphate, therefore, there can be no possible danger in using these salts in the bowel. They have demonstrated that hypertonic solutions of these salts increase in volume and decrease in concentration approaching the blood level. Solutions of concentration nearly iso-osmotic with the blood show little change in volume. Hence there is free passage of water with no diffusion of the sulphates. Sodium chloride solutions on the other hand diffuse freely from gut to blood and vice versa. In cases of extreme atony, I used sodium sulphate and found it produced painful contractures without much result in producing defecation. Equal parts of a 25 per cent solution of magnesium sulphate and sodium sulphate have, on the other hand, given us very remarkable results in producing defecation in many cases of atony of the recto-sigmoid apparatus, pelvic and iliac colon.

During the past year we have been using this method as a routine treatment in atonic cases of long standing and find that in many cases restoration of the contractile power of the recto-sigmoid apparatus and pelvic colon occurs. The more severe forms of atony of the rectum with complete absence of the recto-sigmoid apparatus are greatly benefited by a daily enema of the combined salts. This enema is also of great value in postoperative atonic conditions of the lower colon.

DISCUSSION

DR. FRANK SMITHIES, Chicago: While we all admit that there is a "recto-sigmoid apparatus," while we all suspect that there are changes in pressure in the small and the large gut (such phenomena daily come within one's practical experience) yet it seems to me that we must use a certain amount of restraint, diagnostically and therapeutically when the estimation of such pressure changes, particularly the musculature of the alimentary tract, is deduced from so-called departures from the normal as is shown by roentgen pictures. The roentgen *progress meal*, for example, brought forward as showing points of spasticity, or atony, does not excite normal physiologic responses from the time it passes the lips until the time it goes through the anal sphincter. It is a meal which does not excite secretion psychically, as the result of mass or by local digestive stimulus. It is a meal which is small in bulk compared to its weight and which quickly goes out of suspension as suspending media are digested, consequently, in its passage from the lips to the anus we have the possible introduction of artefacts; these are a serious drawback to proper interpretation of variations in pressure, stasis, spasticity or atony as judged by roentgenograms. If roentgenograms are to be used for such purposes, it seems to me highly desirable that we have a meal which the patient likes, which has gustatory appeal, which is a real food and which can be followed through his alimentary tract during the normal time of digestion; taking into account the normal diminution in volume, consistency and bulk such as occur when food and not a semi-solid, pasty foreign body is introduced into the digestive, absorptive and evacuator machine. Further, such meal should be followed fluoroscopically; it is important that the same individual be put through the same routine a number of times and his roentgen pictures compared and contrasted. He should then be compared and contrasted with a group of similar individuals, from the roentgen, chemic and nutritional viewpoints.

A few years ago, at Boston, we showed a great series of pictures with the spasticities, with the dilatations, with all the evidences of atony, etc., as shown roentgenologically in individuals who were perfectly normal; who had never had a complaint. We similarly showed plates of individuals who had intestinal stasis and who had diarrhea. At that meeting, we requested that men interested in this kind of work indicate from the plates what the clinical symptoms might be in the various unmarked groups of plates. It could not be done, even by many experts in the art who chanced to be present. With the exception of the tremendous congenital dilatation, redundancies and real ptoses if one does not watch the progress of these examples fluoroscopically, there is a great chance for error. When one attempts interpretation of colon plates he must remember that the material is being introduced into the gut the wrong way, i.e., against the normal current. The physiologic stimulus to intestinal movement advances from above downward and not from below; consequently many colon injection plates exhibit the degree of resistance of the gut to a current of barium mixture moving the wrong way under pressure greater than that of the normal intra-colonic force tending to repel the introduction of this foreign substance. If anybody does not comprehend the significance of this, let him inject a quart of ordinary water into his rectum and note the result.

DR. HORACE W. SOPER, St. Louis (closing): Efforts at standardization have been made in many of these cases. The bismuth is incorporated with the evening meal simply mixed with milk, and taken at the end of the meal. Of course, as Dr. Smithies points out, one can draw all sorts of conclusions from X-ray plates of the colon, but at the same time there are certain definite types that can be worked out, and they can only be worked out by means of X-ray plates. We have a large number of plates exhibiting this sort of thing, and every effort has been made to throw out the artefacts and to get the thing down to a real, definite basis. The different types of colon, the contractures that not only can be shown with care by means of the X-ray plate, but can be made out by sigmoidoscopic study of the lower bowel, so that the thing can be corroborated. And I am sure that as time goes on, we will come to a definite recognition of various types of atony of the colon.

THE INCIDENCE OF CECAL TUBERCULOSIS WITH PULMONARY TUBERCULOSIS

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The subject of tuberculosis is particularly interesting to the gastroenterologist, as digestive symptoms are so frequently the first manifestation of early lung involvement. Then throughout the entire course of the disease, a good gastrointestinal tract is almost a *sine qua non* for recovery. To build up the body resistance, an abundance of good nourishing food must be digested and assimilated. If a tuberculosis patient, who has been progressing favorably as far as his pulmonary condition is concerned, reaches a period of standstill or begins to lose ground, there is likely, especially if associated with gastrointestinal symptoms, to be an involvement of the alimentary tract. These symptoms are anorexia, slight bloating, belching, intestinal discomfort or pain usually localized in the mid or lower abdomen. The pains are crampy in character suggesting gas pains and come on at irregular intervals and are likely to be aggravated by eating. There may be fever not due to the lung condition; also, alternating diarrhea and constipation.

Tubercular colitis is by no means an infrequent complication of pulmonary tuberculosis. Pathologists tell us that from 70 to 90 per cent of all tubercular patients show involvement of the gastrointestinal tract, and Albrecht (1) states that with cavity formation practically all do. It is interesting to note that even Hippocrates (2) recognized the seriousness of diarrhea in consumption, for he says in his Aphorisms, "diarrhea attacking a person affected with phthisis is a mortal symptom." The site of the ulcerative lesion, as found by Fenwick and Dodwell (3) in 500 autopsies, was as follows: Ileo-cecal region, 85 per cent (confined to this region alone, 10 per cent); jejunum, 28 per cent; duodenum, 3.4 per cent; ascending colon, 51.4 per cent; descending colon, 21 per cent. The cecum is probably the part first involved, and the process extends in both directions. As to the method of infection, it may be either direct from swallowed sputum or the bacilli may be carried by the mesenteric vessels.

Ileo-cecal tuberculosis in its early stages, at least, is difficult to diagnose by the ordinary clinical methods: Neither the symptomatology, physical examination nor the ordinary laboratory findings give the necessary information. The history points to gastrointestinal tract involvement but does not differ materially from that of other conditions, like chronic appendicitis and the non-tubercular forms of colitis. Alternating constipation and diarrhea, while suggestive, are not always present. Physical examination elicits sensitiveness in the cecal region and frequently, especially late in the disease, a thickening or tumor can be palpated. Likewise, the laboratory findings are of little value. The presence of tubercle bacilli in the feces does not establish the diagnosis, as it has been shown that they exist in the gastric and intestinal contents of patients with pulmonary tuberculosis without any intestinal involvement. Given, then, a patient with pulmonary tuberculosis, exhibiting gastrointestinal symptoms associated with some pain and thickening in the ileo-cecal region, the evidence is favorable to the diagnosis of intestinal tuberculosis. If alternating diarrhea and constipation are also present, the diagnosis is almost certain. But to wait until the fully developed symptom complex is present before making a diagnosis is like refusing to diagnose cancer of the stomach until lactic acid and Boas-Oppeler bacilli are found in the gastric contents and a palpable tumor present. The early diagnosis of the former is just as important as the latter.

Stierlin (4) of Basle was the first to call attention to the Roentgen diagnosis of ileo-cecal tuberculosis. In 1911 he reported 6 cases, 4 of tubercular colitis, 1 of cancer and 1 of ulcerative colitis in which he was unable to fill the cecum and descending colon with the opaque meal. All of the cases were operated upon and the Roentgen findings verified. He says in the main, in infiltrating and ulcerative involvement of the cecum and ascending colon there is an absence of the normal shadow of this part of the colon, as shown in the skiagram 6 or 7 hours after the barium meal, while the terminal ileum and transverse colon are filled. Consequently, the early, as well as the later stages of the so-called cecal tuberculosis can be diagnosed by this means, even in cases undiagnosable by the ordinary clinical methods.

In 1912, Case (5) in a paper discussing tuberculosis of the ileo-cecal region says: "Ileo-cecal tuberculosis is a condition which in a certain number of cases can be almost surely diagnosed by the X-ray examination."

In 1917, Pirie (6) of Montreal at the request of Dr. Archibald (10) made some X-ray studies of intestinal tuberculosis. His report is worth quoting:

Dr. Archibald has asked me if I could write from memory a summary of my findings in tuberculosis conditions of the intestines. I do so with pleasure, as it was about the most interesting work I did for about a year before the war began. Writing as I do without notes from a base hospital in France, I well remember the disappointment we had as in several successive cases of tuberculous cecum I failed absolutely to help in the diagnosis. Some bad luck seemed to dog my steps, for whereas we had formerly been able to show by means of a barium meal the position, shape and size of the normal cecum, yet we failed, in these tuberculous cases, to catch the cecum at the proper time when it was filled by the meal. Finally, the cause of our failure struck us. We could not show the cecum filled by a barium meal because it never did fill when tuberculous ulceration existed. Setting out with this as a working hypothesis, we examined the cases at half-hour intervals from four to twelve hours after the barium meal. We found our theory correct in each case of tuberculous cecum, namely, the cecum never filled up with the meal. Each small squirt of barium that left the ilium was quickly passed on past the cecum and collected elsewhere in the large colon, either in the transverse or the descending part. So that our conclusion was, that in a tuberculous subject with symptoms suggesting tuberculous cecum, if the cecum did not fill from four to twelve hours after the barium meal when examined at intervals of about half an hour, then this want of filling confirmed the diagnosis. On the other hand when it did fill as it does in a normal individual, it negated the diagnosis of tuberculous cecum. We had this latter experience confirmed in one case where a clinical diagnosis of tuberculous cecum had been suggested: The X-ray showed a cecum filled by barium, and at operation a non-tuberculous cecum was found.

It was not, however, until 1919 when Lawrason Brown (7) and Homer Sampson, of the Trudeau Sanatorium, published their work on the Early Diagnosis of Ulcerative Tuberculous Colitis that this subject received the attention it deserves. They observed a large number of cases and confirmed in toto the work of Stierlin and Pirie. Of their 175 cases of pulmonary tuberculosis examined, 44 were positive, and, of these, 28 were operated upon and 27 were found to be correctly diagnosed. Since then, Carmen (8) from the Mayo Clinic and others have added to the literature of this subject. The severity of the lung involvement does not necessarily correspond with that of the intestine. The former may be very slight, even arrested, while the latter extensive and active. Pässler (9) in 1911 reported 2 cases of extensive colon involvement running an acute course and terminating in death with very little lung involvement.

Our paper is based on a study of 80 cases of tuberculosis, examined roentgenologically. Seventy of these are patients at the Onondaga

County Tuberculosis Sanitarium; the majority having fairly well advanced lesions. We have also in our routine work examined about 4000 patients, and have especially during the past year observed the colon very carefully. (See tabulations on pages 58-63.)

TECHNIQUE

With few exceptions the barium enema (Holzknecht's formula) was employed. If the entire colon filled, we assumed that the case was negative, although we knew that slight lesions might be present despite a completely filled colon. These cases, which failed to fill, we had return for an opaque meal, which consisted of 4 ounces of barium suspended in a pint of malted milk thickened with cornstarch. Six hours later the patient presented himself for observation, having abstained from food in the interval. Observations were made at half-hour intervals until we were satisfied that the cecum either could or could not be filled. We only classed those cases as positive, which gave an incomplete filling by both methods. With the enema, pressure with the palpating hand, fails to keep the barium in the involved portion of the colon. When it is forced in, as soon as the pressure is removed, it rapidly shoots out, the uninvolved portion remaining filled. All patients were examined fluroscopically, and plates were taken as a matter of record.

At Trudeau, Brown and Sampson prefer the barium meal, while Carmen at the Mayo Clinic on the other hand prefers the enema, claiming that the small filling defects can better be determined by this method. In our work, we found no discrepancy in the two methods. Of our 80 cases, 12, or 15 per cent, were positive showing a definite filling defect in the cecum or ascending colon. In our 4000 non-tuberculous cases we were not always able to visualize a completely filled colon, but in each instance there was a definite reason for the failure like carcinomatous infiltration, adhesions or pressure from a neighboring tumor. Also in Achylia Gastrica, after a barium meal, in cases associated with diarrhea, we encountered a distinct hypermotility, and as a result the barium was forced along so rapidly that a completely filled cecum could not be observed. A contrast enema, however, accomplished this and differentiated the condition from intestinal tuberculosis. We believe with Stierlin (4), etc., that the filling defect is the most important roentgen sign of cecal tuberculosis. How much of the deformity is due to infiltration, and how much to reflex spasm, cannot be determined by the roentgenologist. When

NAME	CASE NUMBER	AGE	TYPE TUBERCULOSIS	GASTRO-INTESTINAL SYMPTOMS	CONTRAST ENEMA	BARIUM MEAL
Conway, T. E.	1	25	Bilateral, 3 years	Indefinite pains; epigastric; occasional distress after meals	Normal colon filling	
Bludzius, V.	2	42	Bilateral, 2 years	Belches gas; nausea; distress; gastric; 30 minutes p.c., occasional pain in lower right and lower left quadrants	Colon refuses to fill beyond mid-transverse colon; gas outline normal	
Leonard, M.	3	45	Bilateral, 3 years	Gastric pain immediately after meals	Normal colon filling	
Park, G.	4	48	Bilateral	Gas and sour stomach; constipation	Normal colon filling	
Ott, W.	5	22	Bilateral, 3 years	Negative	Normal colon filling	
Dimitroff, W.	6	32	Right pulmonary involvement 1 year	Bowel movement 3 times a day; otherwise negative	Cecum could not retain barium	6 1/2 hours hypermotility; all parts of colon filled; ileal stasis; cecal defect
Pavlow, P.	7	39	Bilateral, 2 years	Occasionally has gastric distress	Reverse peristalsis; backed up in transverse colon	
Flaherty, W.	8	30	Left-sided pulmonary cavity, 6 weeks	Negative, gastric	Could not retain	
O'Malley	9	41	Right-sided, 1 year	Negative, gastric	Normal colon filling	
Skoda, S.	10	28	Bilateral, 5 months	Alternating diarrhea and constipation; right-sided pain; gastric distress p.c.	Cecum would not hold barium; backed up in mid-transverse colon	8 hours shows cecal defect; head of barium in mid-transverse colon; small ileal rest
Sheedy, J.	11	21	Bilateral, 3 years	Intestinal colic at indefinite intervals	Normal colon filling; shows ileo-cecal valve incomplete	
Bugna, A.	12	29	Right-sided, 7 months	Negative	Normal colon filling	
Haase, W.	13	41	Left-sided, 1 year	Diarrhea 6 to 7 times a day	Cecum irritable; could not retain barium; would expel as soon as filled	Ceco-colic defect; hypermotility; ileal stasis
Carlan, J.	14	59	Left-sided, 2 years	Negative	Normal colon filling	
Keefe, J.	15	41	Bilateral, 7 months	Constipated 15 years ago had diarrhea, lasting 2 weeks	Normal colon filling	

Mtoczkooski, A.	16	28	Left-sided, 10 months	Recently has had some gastric pain; last 6 weeks has had bowel movement 5 to 6 times a day	Cecum appears ragged; remainder of colon normal	6½ hours after; one-third stomach rest; ileal stasis; cecal defect; hypermotility of barium in colon
Sterling, M.	17	40	Bilateral, 5 years	Negative	Normal colon filling	
Gorman, W.	18	47	Right-sided, 3 months	Negative	Could not retain enema	
Andrus, F.	19	19	Bilateral, 6 months	Negative	Normal colon; ileo-cecal valve incompetency	
Ward, R.	20	17	Right-sided, 6 months	1-week's diarrhea summer of 1920; now has right lower quadrant pain; otherwise negative	Ragged cecum; ileo-cecal valve incompetency	6½ hours after; two-thirds stomach rest, ileal stasis; cecum spastic; hypermotility
Karpinsky, J.	21	39	Bilateral, 1 year	Has pain more or less constantly in upper right quadrant; frequent attacks of diarrhea; 5 to 6 times a day last few weeks	Normal colon filling	6½ hours hypermotility; all parts of colon filled; cecum shows no marked filling defect
Klase, A.	22	30	Bilateral, 20 months	Belching of gas; heartburn, hunger pain; mucus in stools	Cecum would not hold barium	
Flack, V.	23	16	Spine, 2 years	Negative	Cecum, just gas filled; normal contour	
Pittito, C.	24	25	Left-sided, 2 months	Negative	Normal colon filling	
Ryan, B.	25	36	Bilateral, 4 years	Negative	Cecum, spastic, thinned out; ileo-cecal valve incompetency	
Feely, J.	26	45	Bilateral, 2 years and 3 months	Sour stomach; nausea and vomiting; occasionally has had diarrhea	Normal colon filling	
Davenport, M.	27	31	Right-sided, 10 months	Negative	Normal colon filling	6½ hours; small stomach rest; marked ileal stasis; cecum not filled
Steidle, C.	28	39	Bilateral; larynx involved, 1 year	Negative	Normal colon filling	
Castralli, T.	29	22	Right-sided, 4 months	No appetite; alternating constipation and diarrhea	Normal descending and transverse colon; cecum would not retain barium	

NAME	CASE NUM- BER	AGE	TYPE TUBERCULOSIS	GASTRO-INTESTINAL SYMPTOMS	CONTRAST ENEMA	BARIUM MEAL
McAvilife, G.	30		Bilateral, 3 years	Has sour stomach; bothered with gas; heartburn; one attack of dysentery (blood and diarrhea 2 years ago)	Normal colon filling	
Johnson, H.	31	58	Bilateral, 9 months	Negative	Normal colon filling	
Cullem, P.	32	52	Bilateral, 6 months	Negative	Normal colon filling	
Trant, M.	33	49	Left-sided, 7 months	Negative	Normal colon filling	
Orseni, S.	34	29	Bilateral, 2 months	Negative	Normal colon filling	
Shamrock, A.	35	21	Left-sided, 9 months	Negative	Normal colon filling	
Ringo, J.	36	25	Right-sided, 1 month	Occasionally has had cramps	Normal colon filling	
Detezik, A.	37	35	Bilateral	Constipated; poor appetite; vomits after eating meat	Normal colon filling	
Boyle, J.	38	56	Bilateral, 4 years	Diarrhea once a year during summer	Spastic cecum; ileo-ceca valve incompetency	
Thomas, W.	39	38	Right-sided	Constipation.	Normal colon filling; ileo-cecal valve incompetency	
Kowalski, J.	40	30	Bilateral, 3 years	Negative	Normal colon filling; ileo-cecal valve incompetency	
Heaney, P.	41	45	Bilateral, 1 year	Constipation last 15 years	Normal cecum; spastic descending colon; ileo-cecal valve incompetency	
Pare, E.	42	35	Larynx, 4 months; right-sided pulmonary, 1 month	Negative	Normal colon filling	
Hable, F.	43	40	Tuberculosis of symphysis pubis; right-sided pulmonary; 2 months	Constipated	Cecum irritable; gas filled; normal contour	
Thowalze, K.	44	50	Bilateral, 1 year	Has occasional gastric pain	Normal colon filling	
Leonardo, T.	45	21	Right-sided pulmonary tuberculosis; abscess of cheek	Negative	Normal colon filling	

Howe, Miss E.	46	16	Glands of neck, 1 year; pulmonary tuberculosis, 1 month	Negative	Normal colon filling	6½ hours after; ileal filling; spastic cecum
Spencer, Mrs. B.	47	22	Bilateral, 3 years	Negative	Cecum spastic; unable to retain barium; reverse peristalsis Normal colon filling	6½ hours after; cecal defect and spasm of ascending colon
McGree, Miss E.	48	35	Bilateral, 1 year	Constipation	Normal colon filling	6½ hours; one-half in ileum and one-half in ceco-colon
Kelly, E.	49	33	Left lung, 4 weeks	Appetite poor; otherwise negative	Normal colon filling; ileo-cecal valve incompetency	6½ hours; one-half stomach rest; remainder in ileum; cecum not filled
Griffiths, Mrs. S.	50	66	Bilateral, 16 years	Belches gas; distress after	Spastic cecum; irritable; would not hold barium	6½ hours after; small stomach rest; ileal defect; spasm; hypermotility
Hubbard, Mrs. A.	51	39	Bilateral	Constipated	Dilated cecum; no caustations	6½ hours after; small stomach rest; ileal stasis; spastic cecum
Collins	52	43	Bilateral	Constipated at present; borborygmi; occasional colic; 6 years ago had diarrhea lasting all year	Could not retain	6½ hours after; small stomach rest; ileal stasis; spastic cecum
Elizabeth, Miss F.	53	21	Right-sided, 5 months	Bloats after meals; belches considerable gas; has gas pains; frequently has nausea	Ceco-colon would not fill	6½ hours after; head of barium in mid-transverse colon; normal ceco-colon
Wamby, Miss L.	54	23	Left-sided, 11 months	Belches gas p.c.	Normal colon filling; ileo-cecal valve incompetency	6½ hours after hypermotility cecal defect; small amount in ileum
Leibold, Miss A.	55	14	Bilateral, 3 years	Negative	Cecum apparently normal; marked ileo-cecal valve incompetency	7½ hours after; shows small cecal defect
Parker, Dr. A. C.	56	45	Left-sided, 7 years	Nausea; periods of diarrhea alternating with constipation	Spastic irregular cecum as far as mid-transverse colon; remainder normal	6½ hours; small stomach rest; head of colon; splenic flexure; normal ceco-colon
Knaube, Miss F.	57	57	Bilateral, 1½ years	Constipated occasionally has pain lower right quadrant	Normal colon filling	

NAME	CASE NUMBER	AGE	TYPE TUBERCULOSIS	GASTRO-INTESTINAL SYMPTOMS	CONTRAST ENEMA	BARIUM MEAL
Rocket, Miss M.	58	32	Left-sided	Distressed with gas; constipated; 1 year ago had diarrhea lasting 3 to 4 days	Normal colon filling; ileo-cecal valve incompetency	6½ hours; all of barium massed in terminal ileum
Johnson, A.	59	22	Right-sided (left), 3 weeks	Negative	Normal colon filling; ileo-cecal valve incompetency	6½ hours; ileal rest; no barium in ceco-colon
Fisher, A.	60	37	Bilateral, 2 months	Poor appetite; alternating constipation and diarrhea		6 hours; ileal rest; no cecal defect
Luczycki	61	40	Left	Bloated after meals; great deal of belching and heartburn; distress following meals; constipation	Normal colon filling	Normal
Wood, Mrs. J.	63	66	Bilateral, 2 years	Constipation		6½ hours; one-third stomach rest; part in jejunum, remainder in colon; no ceco-colon defect
Petonyak, Miss C.	64	23	Bilateral, 5 years	Negative		6½ hours; two-thirds stomach rest; spastic colon
Easlick, Mrs. S.	65	27	Bilateral, 5 months	Negative		6½ hours; one-third stomach rest; negative ceco-colon
Murphy, Mrs. N.	66	28	Left lung, 2 years	Belches gas		6½ hours; all of barium massed in terminal ileum
Mahar, Miss E.	67	19	Right-sided, 2 years	stipated		
Woods, Miss H.	68	44	Right sided	Diarrhea 4 and 5 times a day; occasional periods of constipation		
Drury, Mrs. E.	69	33	Bilateral, 2 months	Constipation		6½ hours; ileal stasis; cecum shows slight defect
Clerc, R.	70	37	Bilateral, 2 years	Occasional lower right quadrant pain		9 hours; small stomach rest; cecal defect; hypermotility; ileal stasis
Kuhn, G.	71	24	Bilateral, 2 years	Gas in stomach; diarrhea every day	Cecum would not hold barium spastic; irritable; small amount would be expelled as soon as it entered	7 hours; no barium visualized at any time in cecum

Cerkendall, J. Mersha, F.	72 73	42 42	Bilateral Bilateral, diabetes	Appetite poor; constipation Some distress following meals; occasional attacks of diar- rhea; usually constipated Negative	Normal colon filling Normal colon filling	7 hours; ileal stasis 6½ hours; stomach empty; mass of barium in terminal ileum 7 hours; head of barium in mid-transverse colon; no cecal defect Normal
Kenyon, Mrs. L.	74	39	Bilateral	Upper right quadrant dis- tress; constipation Acute pain right upper quad- rant	Normal colon filling	6 hours; head of barium in no barium in cecum 8 hours; head of barium in splenic flexure; no cecal defect
Zarkardi, J. J. May, Miss F.	75 76	51 30	Bilateral Right-sided	Constipation Constipation	Normal colon filling	6 hours; stomach empty; mass of barium in terminal ileum; no barium in cecum 8 hours; head of barium in mid-transverse colon; no barium in ileum; no cecal defect
Curtiss, W. Arbeit, Miss A.	77 78	47 66	Bilateral	Constant pains in pit of stom- ach; continual heartburn; has had occasional attacks of diarrhea Constipation	Normal colon filling	6 hours; stomach empty; cecum well filled; ileal stasis; head of barium in mid- transverse colon 6 hours; stomach empty; some ileal stasis; no cecal defect
Bigsby, Miss F. Burns, F.	79 80	21 62				

marked thickening and contraction has taken place, there may be obstruction.

We were surprised by the frequency of gastric hypomotility; barium frequently remaining in the stomach seven and eight hours after the ingestion of the meal. This has a practical bearing on the treatment of pulmonary tuberculosis, as a few years ago forced feeding was considered an essential element for recovery. To force-feed a stomach unable to dispose of an ordinary meal is illogical. The over-filled stomach may cause the anorexia, distention and fermentation so frequently complained of and explains why these patients give up one article of food after another, believing that it is the food eaten at the last meal which causes the disturbance, whereas in reality it is due to the fermentation of the food remaining in the stomach from previous meals that is at fault. The meal must not be greater than the stomach can propel into the small intestine before the next meal is partaken. In our contrast enema studies, we were impressed by the frequency of ileo-cecal incompetency (25 per cent). In 70 per cent there was a marked ileal stasis. All of our positive cases were sensitive in the cecal region, but in none was a definite tumor palpable. In the symptomatology, our patients volunteered the information that they felt weak and prostrated after a bowel movement, and also that the odor of the stool was very foul and penetrating.

In their first report, Brown (7) and Sampson laid considerable stress on hypermotility of the colon as a sign of tuberculous colitis. There is, however, no true hypermotility, but rather a rapid passage of the colonic contents through the involved area due to rigidity of the infiltration or the contraction of the spasm.

It must, however, be borne in mind that roentgenology does not diagnose tuberculosis of the intestines, as the same findings occur in cancer and ulcerative colitis as mentioned by Stierlin (4). Roentgenology should not be required to make a pathological diagnosis—this should be reserved for the pathologist. Roentgenology is nothing but inspection, and as such is a part of clinical medicine. Sufficient evidence is now at hand, however, to warrant the inference that a filling defect in the cecum or ascending colon in a person afflicted with tuberculosis and associated with gastrointestinal symptoms is almost always indicative of tuberculosis of this area. We have then in roentgenology a very important aid in the diagnosis of tuberculous colitis. The importance of the early diagnosis cannot be over-emphasized, as only then can treatment be of avail. Mild lesions sometimes heal

spontaneously. Drugs are of no value. Surgery in the hands of qualified operators has given very satisfactory results, even in advanced cases. The recent reports of Archibald (10) and Paterson (11) emphasize this. X-ray, radium, and more recently heliotherapy in the form of the quartz lamplight are being used extensively, the latter especially at Saranac.

We wish to take this occasion to express our thanks to Dr. H. J. Brayton for the privilege of examining the patients at the Onondaga County Tuberculosis Sanatorium, which forms the main basis of this paper.

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DISCUSSION

DR. LUDWIG KAST, New York: I would like to ask Dr. Levy whether he has found it of value in his diagnosis of abdominal tuberculosis to analyze the types of abdominal pain in those cases in which abdominal pain existed. My question is prompted by the observation which I made six or seven years ago on a woman of about fifty years of age who showed a peculiar type of abdominal pain, and since that I have seen it in cases of abdominal tuberculosis. The patient had in the beginning of her ailment attacks of pain in the lower right quadrant every few days, lasting from half an hour to two or three hours. The pain had no characteristic radiation and was not characteristic in any way. Gradually the pain increased in frequency and severity. The diagnosis of appendicitis was made and the patient was operated upon. The diagnosis, as I understood it at that time, was adhesions from fibrous appendicitis, and for about three or four weeks, perhaps a little longer,

the patient felt much better, and then these attacks of pain came again regularly in the latter part of the afternoon, lasting three or four or five hours. They became so severe that she required morphia. The case puzzled us for a long time, and she was seen by a number of men in New York. It was complicated by the fact that she had a moderate right pyelitis. The diagnosis was based on the fact that the pain came in the afternoon with a slight rise of temperature. The case turned out to be one of tuberculosis of the ileo-cecal region, which was not found at the time of the first operation. Since that time I have seen cases of abdominal tuberculosis with the regularly appearing pain and temperature, and that gave an indication of the tuberculous nature.

DR. THOMAS R. BROWN, Baltimore: I have had the opportunity of seeing similar cases to those mentioned by Dr. Kast. The first one had been operated upon for a pelvic condition, and then she developed an appendix attack with leucocytosis of 13,000 and that subsided and she was not operated upon. Subsequently she developed the same clinical history as Dr. Kast described. Finally she had a large intestinal hemorrhage, and a resection was made, and the tuberculous ileotyphlitis was determined; and the second case was practically the same except for the absence of hemorrhage.

DR. I. H. LEVY, Syracuse (closing): Dr. Archibald has also called attention to the occurrence of pain late in the afternoon in these cases; and we have observed the same phenomenon.

INTERMITTENT HYDRONEPHROSIS WITH GASTRO-ENTEROLOGIC SYMPTOMS

ALEXIUS McGLANNAN

Baltimore, Maryland

For a long time hydronephrosis has been known as the great mimic in abdominal pathology. The mass in an upper quadrant of the abdomen has been mistaken for a distended gall bladder, a cyst of the pancreas and various other tumors.

The changes of urinary function in hydronephrosis are seldom great. Ordinarily the disease is unilateral and therefore systemic indications of urinary disturbance are rarely present. The tumor may never be large and during the periods of remission or intermission may become so small as to escape notice.

Disturbance of gastrointestinal function may be the only constant feature of the condition. Dietl's crisis, characteristic of movable kidney and believed to have its origin in a vascular or ureteral obstruction, points out a reflex relationship between the urinary and alimentary organs.

Gastro-enterological symptoms therefore may become of the greatest importance in the course of an intermittent hydronephrosis. The possibility of the condition must be borne in mind whenever a confusing set of symptoms can not be explained by the presence of a clearly identified lesion of the alimentary tract or its associated organs. Under such circumstances a complete urological examination including catheterization of the ureters, measurement of the capacity of the pelvis, determination of the function of both kidneys, and pyelograms will prove the presence or absence of a hydronephrosis.

Early in the course of the disease, conservative operations varying from dilatation of a strictured ureter to plastic anastomosis between this tube and the pelvis of the kidney, are to be performed. Late in the disease, when the accompanying progressive sclerosis of the pelvic walls and the kidney parenchyma has seriously impaired the function of the organ, nephrectomy is indicated. Before resorting to this radical operation, however, the possibility of improving the function of the kidney, after the pressure has been relieved, should be con-

sidered. This point may become of great importance when the condition of the other kidney is also below normal.

Hydronephrosis is not a rare lesion, and the 2 cases now reported are brought to your attention only because the gastro-enterological symptoms are so prominent in their clinical course.

Case 1. S. 1836. The patient, a white boy, age thirteen, was admitted to St. Agnes' Hospital, June 11, 1908, on account of recurring pain in the abdomen, with nausea and vomiting and constipation. The symptoms had been present ten years. The boy had been studied by several eminent clinicians, but no diagnosis had been made.

The attacks came on without any relation to the taking of food, at intervals of about two weeks, and lasted from twenty-four to forty-eight hours. During the attack there was bulging of the left side of the abdomen, with a ball-shaped swelling at the outer border of the left rectus between the umbilicus and the anterior superior spine. The pain was colicky and referred to the region of the ball-shaped swelling just described, and to the costal margin in the left mammary line. The pain did not radiate in any direction. Recovery from the attack was prompt. Usually the next day the boy was able to go to school. During the interval he was entirely well.

Examination of the abdomen revealed a small bulging at the outer border of the left rectus muscle at the level of the umbilicus. Pressure at this point brought out gurgling and a sense of splashing. No other masses or areas of resistance could be felt. A peristaltic wave was seen passing downward with respiration from the tip of the xiphoid across the abdomen.

Dilatation of the bowel with air through a rectal tube showed even distension, except in the region of the cecum. As the bowel became distended, the patient complained of pain in the left flank, similar to the pain during an attack.

Bismuth X-ray showed a break in the shadow in the descending colon just above the sigmoid. This was attributed to air or feces in the bowel. At the time of this examination (1908) our limited experience did not permit us to make any deductions from the X-ray plate. Sigmoid volvulus, or congenital dilatation of the colon were considered as possible causes for the symptoms.

The blood count was normal and there were no pathological changes in the several specimens of urine examined.

While in the hospital the boy had an attack. Considerable bulging of the left flank was noted. The colicky pain was severe. The ball-like mass at the edge of the rectus was tender. There was frequent desire to urinate and a considerable quantity was passed with each voiding. As the attack subsided the bulging of the flank disappeared.

After this attack the possibility of an intermittent hydronephrosis was considered, as a cause of the boy's illness.

On July 3 Dr. Bloodgood opened the left flank behind the peritoneum at the level of the umbilicus, by a muscle splitting incision. The moderately distended sac of hydronephrosis was identified and brought up to the surface. The wound was partially sutured and then iodoform gauze was packed around the sac to wall off the other tissues. The sac was opened by a minute incision. Urine began to flow at once.

The wound gradually healed, and closed down to a pinhead-sized urinary fistula situated in the flank. This fistula drained for nearly two years. At the end of that time, it was closed by separating the sac from the abdominal wall and plicating it until the several layers made a band of tissue about $\frac{1}{2}$ inch wide firmly fixed against the side of the kidney. This maneuver was successful. The wound healed without complications and there was no more leaking of urine. The patient is now a vigorous and active young man, cured eleven years.

Case 2. S. 20695. The patient, a white female, age seventeen, was admitted to the Mercy Hospital January 13, 1921, on account of constant pain in the abdomen, with nausea and vomiting. There were paroxysmal exacerbations of the pain. She had suffered from attacks of acute indigestion for some time, but a routine physical examination made in May, 1920, did not reveal any massive or tender areas in the abdomen.

The present attack had begun about two weeks before admission with acute indigestion followed by diarrhea and pain in the upper left quadrant. At the time of admission there was a disc-like mass about the size of a silver dollar, just under the outer edge of the left rectus muscle, about 2 inches above the umbilicus. This area was tender and was flat on light percussion. This disc-like mass was considered part of a larger smooth, firm swelling which extended upward to the costal margin and outward to the anterior axillary line. The large swelling was regular in outline and moved with respiration and from side to side. The tender area was taken to be a mass of omentum plastered over a slowly leaking gastric ulcer and binding it to the abdominal wall. The stomach contents were free from blood and contained less than the normal quantity of acid.

X-ray study showed a dilated stomach with a remarkable zone into which the bismuth did not penetrate. The colon picture was negative. The gastric shadow was interpreted as one due to extra-gastric tumor behind the stomach, or a polypoid growth within the organ.

A few days later the pain became much less severe and we noted that the mass in the flank had become smaller. Later the mass recurred and with it the pain. We then felt reasonably certain that we were dealing with a hydronephrosis.

The urological study made by Dr. A. J. Gillis showed a phthalein output of less than 5 on the left and of 45 on the right side. There was some difficulty in passing the catheter through the left ureter. The sodium iodide pyelogram showed clearly the dilated ureter and the swollen pelvis of the kidney.

Because of the low phthalein output of the left kidney and the good output of the right one, we decided to remove the functionless kidney rather than risk a urinary fistula in the attempt to do a plastic operation.

Operation, January 24, 1921. McGlannan. Anesthetic, nitrous oxide. The mass was exposed by a lumbar incision. The sac was aspirated and 550 cc. of fluid recovered. The kidney and the sac and about 2 inches of dilated ureter were removed. The wound was closed with drainage and healed without any complications. The patient is now well.

Analysis of the fluid from the sac showed it to contain a small quantity of urea. It was free from albumin or sugar. Examination of the sediment after centrifugation revealed a number of poorly staining cells with single nuclei, some bacilli which resembled the colon bacillus. There were no white blood corpuscles present.

Gross pathology. The specimen consists of the kidney, the hydronephrotic sac and about 1 inch of ureter. The ureter is dilated, its walls are thin and the lumen is about 1 cm. in diameter. The sac is thin walled and has a capacity of about 500 cc. The cut surface of the kidney shows a small area of parenchyma at either pole and around the convex border. The greater portion of the kidney is made up of cystic areas which are the dilated calyces. Between these cystic dilatations the tissue is grey and fibrous. The photograph shows the kidney cut open with the hydronephrotic sac attached at the hilum. A thin layer of kidney tissue is shown at the outer edge of the sac.

Through the courtesy of my colleague, Dr. A. Samuels, gynecologist to the Mercy Hospital, I am able to report a third case.

Patient is an Italian woman, age thirty-three, well nourished, has been in this country one year, speaks English very poorly and the following history was obtained through an interpreter who also spoke English very poorly.

Previous history. About three years ago patient had severe vomiting spells with pain in epigastric region. She was operated upon for the relief of this vomiting. She said after the operation the vomiting stopped for a period of five or six months and then it returned.

Pregnancies. Two children, last child year and half ago.

Appetite. Poor, has nausea most of the day and has periodic spells of vomiting.

Micturition. Normal, none during the night.

Bowels. Constipated.

Menstrual history. Last menstrual period about two months ago, flowed four days, no pain.

Present complaint. Pain in epigastric region with vomiting that is not associated with the intake of food. Patient believes that vomiting may be due to a possible early pregnancy.

Examination. Patient has a linear scar above the umbilical which is well healed and not tender on pressure. There is no tenderness over the gall-bladder. Right kidney palpable but not tender. In the left kidney region there is a decided mass, slightly movable and tender on deep pressure. Perineum relaxed, slight cystocele. Uterus retroflexed, normal in size. Not pregnant.

A cystoscopic and renal examination was advised to which the patient consented.

On cystoscopic examination the bladder was found to be normal in color and size, the ureteral openings normal, the catheter passed into the right kidney without any obstruction, also into the left. The dripping from the right kidney was normal, from the left kidney almost a continuous stream. Capacity of right kidney 20 cc., of left kidney 1500 cc. From the constant flow of urine from the left kidney and the large capacity a diagnosis of hydronephrosis was made. Phenolphthalein was given intravenously. The dye appeared in the right kidney in two minutes, none appeared in the left side up to thirty minutes. A pyelogram was taken which showed a normal right pelvis of the kidney and a large hydronephrotic kidney on the left side.

Diagnosis. Hydronephrosis of the left kidney.

Treatment advised. Operation.

Patient was seen three days after ureteral catheterization and has been free of her nausea and vomiting.

DISCUSSION

DR. H. W. BETTMAN, Cincinnati: I have been impressed for many years in studying the histories of many unsuccessful appendicitis operations in people who are rushed to the hospital with the diagnosis of appendicitis and operated upon, in various parts of the country, and the condition was found subsequently to be due to Dietl's crises and stone in the kidney. I have under observation now a young man who served in the Army and they had difficulty in determining whether he had appendicitis and they sent him back to America and he has had severe attacks of pain in the right iliac region in which the urologist called into consultation has found stricture in the left (right?) ureter probably due to the passage of a stone in one of his attacks. This man still had attacks one in three weeks, notwithstanding the fact that the urologist has stretched the ureter.

I can recall my experience one morning at the hospital, being seized with bloating in the abdomen with nausea without cause. This continued for fifteen minutes with abdominal distension followed by vomiting and after that I got the symptoms of urinary calculus and passed an oxalate stone; but the first symptom I had was abdominal distension and nausea preceding any urinary symptoms at all. I think we ought to be on our watch over and over again against diagnosing appendicitis when the symptoms are really in the kidney.

DR. MAX EINHORN, New York: I am very much interested in the paper of Dr. McGlannan. The reflex affections of the stomach due to kidney disturbances are quite well known; and one of the first cases years ago which I saw in this line was one with achylia gastrica with severe symptoms of the stomach but a patient who had a calculus in the kidney. She was after a while operated upon, and after the operation she became free from her gastric symptoms and the chylia disappeared. That was the first one. About two years ago I observed a young man, aged twenty-two, with hydronephrosis. He came to the hospital on account of his stomach, running down in weight and with severe pain. He had a tumor on the right side, and the liver was enlarged, and I could not make out that tumor belonged to the kidney. He was examined at the hospital, and the left kidney was found to be all right. So it was decided to operate on him, and he had a similar condition—hydronephrosis. There was no distinct tumor found and he got well.

Very often the symptoms which bring the patient are those referring to the digestive tract and in reality it is something else, and we must all be aware of that.

DR. JULIUS FRIEDENWALD, Baltimore: It was thirty years ago that Dr. Osler first recognized his first case of intermittent hydronephrosis in a patient who has subsequently fallen into my hands. And according to him it was the first case recognized in this country although Dietl described the condition as early as 1864.

I believe that many of these spastic conditions which are produced by the attack are due to a pylorospasm (pyelospasm?) although in the beginning of the attack we do have pressure in the epigastrium, but I believe that the symptoms of nausea and vomiting and pain are largely due to this pylorospasm, as I have recognized it in the large number of cases in my care.

DR. THOMAS R. BROWN, Baltimore: I think we should call attention to the frequency with which acute pyelitis is mistaken for appendicitis. In pyelitis pus very often does not appear in the urine until twenty-hour hours or longer from the beginning of the attack, and therefore I think it is very important, because it is so frequently overlooked, that urine examinations should be carried on for at least forty-eight hours to determine whether these are cases of pyelitis simulating appendiceal attacks.

DR. ALEXIUS McGLANNAN, Baltimore (closing): The lesson we have learned from studying these patients is that when we have an individual with gastro-enterologic symptoms and a painstaking examination fails to give us a clear cut diagnosis, then we should think of a hydronephrosis and have the patient examined by a competent urologist. The ordinary examination of the urine does not help us. The condition is unilateral. Whatever damage is done to the kidney is done on the side of the hydronephrosis, and the other kidney immediately compensates for it, therefore an ordinary urine examination does not show any change. An examination of the twenty-four-hour specimen may give a clue, but the way to find the lesion is by passing a ureteral catheter and making a pyelogram. We will not take out so many chronic appendices, if we remember chronic pyelitis.

THE ADVANTAGES OF EXAMINING THE FASTING STOMACH IN GASTROINTESTINAL DIAGNOSIS

ERNEST H. GAITHER

From the Digestive Clinic of the Johns Hopkins Hospital

TECHNIQUE

I first became impressed with the paramount importance of the fasting stomach test, while working in Ewald's clinic in 1912. The technique, at that time, was to give a supper consisting of bread and butter, potato, some green vegetable, meat and tea, and then aspirate the stomach contents the next morning—twelve hours after the ingestion of the meal.

Later in the same year, Hausmann described a test which attracted my attention on account of its simplicity and ease of application. Ever since that time we have been working with it and have found it to be eminently satisfactory. The technique is as follows: Twelve hours before the stomach is to be evacuated with the tube, the patient is given 4 tablespoonfuls of rice which has been thoroughly boiled in milk or water, and may be eaten with milk, cream, butter or sugar. As a means of detecting any evidence of obstruction, it was formerly our custom to add raisins, currants, figs, dates or some finely chopped green vegetable, but latterly we have come to regard such additions as superfluous, inasmuch as they do not give us any more information than can be obtained from rice alone.

Twelve hours after this meal, the gastric contents are extracted. If obstruction is suspected, one may easily obtain a clue as to the degree of interference by withdrawing the contents at various intervals.

The specimen is then set aside in a conical glass to admit of sedimentation. If there be a sufficient amount, titration for the acid values may be carried out; but although this has a certain value, it is not so satisfactory as the estimation of acidity after a test breakfast. A qualitative examination for free acid, however, should always be made.

A careful macroscopic inspection is made, after which the supernatant fluid is poured off, and Lugol's and Sudan III solutions are added to the residue; a cover-slip preparation is then made for study.

FASTING CONTENT

Physical characteristics (macroscopical, microscopical)

Invaluable information may be obtained by a study of the physical characteristics of the fasting stomach.

Amount. When the contents obtained are less than 25 cc., we look upon the findings as normal; whereas anything over this amount speaks for hypersecretion, an obstruction, or both, or a regurgitation. This last condition may be of great importance and is recognized by the diminution or lack of acid and by the presence of bile.

Appearance and consistence. In the majority of cases the fluid is colorless or tends to be slightly turbid, with a light feathery floating material, and a flocculent residue which is also colorless. Exceptionally the gastric contents are clear, but as a rule only when enormous quantities due to a hypersecretion are obtained.

The precipitation of mucin by the gastric juice causes the formation of whitish particles, which at times closely resemble starch granules. However, a differential diagnosis may readily be established by the addition of Lugol's solution or iodine, which, in the case of starch, will give a blue reaction, whereas the mucin particles will not be affected by it.

At times, settling to the bottom of the glass, we note a finely granular material, which may be colorless or partake of the color of the contents—yellow or green. This material is unquestionably gastric debris and has no special significance; as in the case of the mucin particles described above, it may be easily identified by the same procedure.

The microscopic supplement to these findings will be dealt with later.

Quite frequently we note a yellowish or greenish color due to an admixture of regurgitated bile. In the former case, the contamination has been recent; in the latter, the bile has been present for a greater length of time, and oxidation has taken place, resulting in the formation of biliverdin. The color may be changed by chromogenic microorganisms. Regurgitation is brought about by muscular contraction, resulting in a marked increase of intra-abdominal and intra-intestinal pressure, which causes reversed peristalsis in the duodenum, regurgitation and a backward flow into the stomach.

The presence of blood may greatly alter its characteristics, a bright red color denoting hemorrhage from ulceration (benign or malignant). Trauma, occasioned by the passage of the stomach tube may some-

times be responsible for a small amount of fresh blood, whereas the coffee-ground or blackish material intimately admixed is indicative of a slow ooze.

The normal fasting content is limpid, and can easily be dropped; but attention should be directed to a frequent error made by students, who often mistake the buccal mucus or swallowed saliva, which floats on the fluid, for true gastric mucus. The former presents a frothy, air-impregnated, thick, mucoid substance which is entirely separate from the true gastric content, and can be easily removed. The characteristics of the latter are entirely different. It is of thick, ropy gelatinous consistence, and is intimately admixed with and inseparable from the gastric secretion—as a matter of fact, it is really the product of the gastric glands. Its presence is very suggestive of a catarrhal gastritis, but occasionally it is indicative of a true gastric myxorrhoea of nervous origin.

In normal cases we never find foreign bodies, such as hairballs, round worms, or particles of food in the form of carbohydrates, fats and starches. Mucus, pus and blood are likewise absent.

Reaction. In the majority of cases, we find an acid reaction, but not infrequently the contents are alkaline or neutral. In our experience, however, the significance of the reaction in itself is relatively unimportant.

Odor. The normal contents have no characteristic odor, but when obstruction has taken place with a resultant stagnation, putrefaction and fermentation, sour, putrid and disagreeable odors are noted. Hydrogen sulphide is at times given off.

Microscopic examination. Before pathological processes have interfered with the physiological functioning of the motor power, several distinct entities in the gastric content are noted microscopically: (1) epithelial cells, from the mouth, fauces and stomach; (2) free nuclei, whose presence is due to the digestive action of the gastric secretion upon the wall and protoplasm of the epithelial cell. These nuclei are apt to become arranged in clumps, and are often mistaken for sarcinae. In the third group, belong the spirals, which are produced as a result of precipitation of the salivary mucin by the gastric juice.

In cases showing little or no free acid, we have noted an excessive number of epithelial and white blood cells (the latter being especially abundant if catarrhal conditions are present in the upper digestive and respiratory tracts). From a negative standpoint, this finding seems to prove the effectiveness of the acid gastric juice in clearing the stomach of detritus whether of cellular or of bacterial origin.

In addition we see various clumps of material having no distinct morphological characteristics. These consist of end-products of digestion, and in addition, inert bacterial and cellular elements.

THE TEST BREAKFAST OR THE EXAMINATION OF THE FASTING STOMACH;
WHICH METHOD GIVES THE MOST VALUABLE AND
RELIABLE INFORMATION?

For some years we have been interested in this problem, and prolonged study has led us to the adoption of decided views which we desire to present for discussion. We have become convinced that it is a gross error to endeavor to build a gastric pathology upon secretory findings, for the reason that there are too many unknown quantities directly affecting secretory functions over which we have no control and which bring about a labile condition whereby the secretion is continually changing quantitatively and qualitatively. For example, we must take into consideration the general bodily resistance and vital capacity which are ever changing according to the physical or psychological strain under which the patient may be laboring at different times and under various conditions. Or again, we must remember quick response of secretion to immediate psychic upsets, such as the thought and act of swallowing a tube; nor should we forget the various incidents leading up to this procedure. Furthermore, the relative amount of gastric mucus and material referable to regurgitation from the duodenum must be reckoned with at the time of examination. And finally, business and household cares, responsibilities producing mental and physical strain, shocks of various kinds, the character of food eaten, focal infections (acting locally or through the general system), reflex disturbances from other organs, malfunction of ductless glands, blood dyscrasias, and innumerable extraneous conditions may produce an unstable and ever-changing gastric secretion.

From the viewpoint of academic interest and as a spectacular procedure, we have no fault to find with fractional gastric analysis; but so far as our experience goes, we cannot but feel strongly that it has no vital diagnostic value, and that it does not give us any more accurate knowledge than can be obtained when the technique as originated by Ewald and Kussmaul is carried out.

The advocates of fractional gastric analysis present a weak case when they start with three normals, for if such be a fact, how may we expect to place the abnormal or pathological reactions with intelligence and exactitude?

Furthermore, against the fractional method it may be urged that a rubber tube and metal body, the former being in direct contact with the mucous membranes of the mouth, fauces, esophagus and stomach, while the latter is applied to the mucous membrane of the stomach for an extended period, must unquestionably act as foreign bodies and irritants and cannot help but produce an unphysiologic response. Certainly there is called forth an excessive secretion of mucus—as evidenced by the amount poured out from the buccal cavity, and we are convinced that an analogous reaction occurs in the stomach.

Another fact upon which we personally lay even more stress is that for diagnostic purpose we have been unable to get any help from the fractional method except possibly in a primary achylia, which later may show an acid secretion; and even in these cases the value of the procedure is problematical.

So far as diagnosis is concerned what information can be gained by showing a curve charted in red or blue ink which, at sixty minutes, may show a free hydrochloric acid of 40 and a total acid of 75; while at seventy-five minutes, the values have dropped back, gone forward, or remained constant? Nor can we disregard the fact that the authors of this method themselves admit that, under normal conditions, at least three and possibly five normal curves may be met with.

A knowledge of the degree of gastric acidity at best can only be comparative and questionable; it can be of positive value only when considered in conjunction with other findings. And although we feel that no procedure should be despised which promises to be of assistance, however slight, in diagnosis; nevertheless, so far as we are concerned, our experience has definitely proved that of all procedures this approximation of acidities—free and total—is the least helpful, and practically may be discarded for other measures which have proved to be of far greater value.

It must be frankly admitted that the whole procedure of gastric aspiration is invariably associated with some unphysiologic results and findings but it is the nearest to normal that we possess.

Except in a small class of cases—notably in achylia with a patent pylorus, which allows of a premature emptying of the stomach or in pylorospasm, in which we have the opposite effect—the motor power in no wise shows the instability which so readily occurs in the secretory functioning. And it is because of this fundamental difference that, for the evaluation of gastric functioning, the knowledge gained by a study of the motor findings must undoubtedly be regarded as the most dependable and valuable.

When a rice retention meal is given at night, all other things being equal, the patient has a chance of obtaining an uninterrupted rest, and nothing occurs which interferes much with the motor function. A quick aspiration will, for all practical purposes, empty the stomach completely, or certainly not leave behind more than a few cubic centimeters.

More than 25 cc. of fasting content is indicative of a pathologic condition. This statement is made only after most careful observation in thousands of fasting stomachs, in which by far the greater majority exhibited a residue of less than 10 cc. Nor does our investigation stop here; for after a careful macroscopic study, a routine but thorough microscopic examination is made.

Some authorities claim that the stomach cannot be completely emptied by aspiration with an Ewald tube. Our experience is in direct variance with this assertion; but in any case it would make no vital difference in the diagnosis if a few cubic centimeters were left behind, always provided that other tests are supplemented by a thorough microscopic investigation—a procedure which we insist upon as being fundamental.

In connection with complete evacuation through the Ewald tube, the following incident may be of interest. A few days ago evidence of complete pyloric obstruction appeared in a patient who was suffering from a carcinomatous growth; he had not been seen for some weeks, and stagnation had taken place, causing putrid material to accumulate. It was thought advisable to lavage the stomach every day for a few days before the operation. At each washing an accumulation of food was noted. The writer was requested to lavage the stomach one hour before operation and when the tube was introduced, a large quantity of muddy-appearing, foul material was obtained. Lavage was performed until nothing more could be obtained. The writer was standing by the surgeon one hour later when an incision 3 inches long was made in the stomach—it was perfectly empty.

HYPERSECRETION (INTRINSIC OR EXTRINSIC IN ORIGIN); METHOD OF DISCOVERY

We regard the finding of 25 cc. or more in the fasting stomach as indicative of hypersecretion or obstruction. As to the physical characteristics of the fluid, it is first necessary to distinguish between *gastro-succorhea* and *gastro-myxorhea*. In the former, it is limpid, is easily dropped, highly acid, colorless, yellow or green with usually

(if no gross retention be present) a light, flocculent residue—a cloudy material or whitish flakes sedimenting to the bottom—while in the body of the fluid, there floats a light whitish or colorless feathery material. If, however, biliary coloring material be present, the whole content may be yellow or green. The usual salivary and air-impregnated mucus floats on the top. The reaction is practically always acid.

Such a material is indicative of an irritative, ulcerative or inflammatory lesion of intrinsic or extrinsic origin; in the former case, it may result from a gastritis (subacute or chronic) or superficial erosion, ulceration, scar tissue or a foreign growth. In addition to their irritating and stimulating effect upon the gastric glands, in the vast majority of cases, such conditions also produce a decided pylorospasm which tends to prevent the egress of the excessive gastric secretion, but may not be of sufficient intensity to cause a gross obstruction. The extrinsic lesions which may produce these conditions, and which should always be considered as possible factors, are: lesions of the gall bladder, including adhesions between this organ, the pylorus and other structures, lesions of the duodenum, appendix, genito-urinary tract, the pelvic organs in females and of the prostate in males.

Nevertheless, it must be insisted that such gastric contents at times are the results of a true neurosis or are merely a gastric manifestation of cerebrospinal disease, for example, *tabes dorsalis*.

By *gastro-myxorrhœa*, we mean a condition in which an excessive secretion of free mucus is in evidence.

The secretion is thick, glairy, ropy, of mucilaginous consistency and cannot be dropped. It is usually colorless, although it may be stained yellow or green by the biliary secretion and is much clearer than the limpid secretion found in *gastro-succorrhœa*. The amount of residue is usually negligible. The reaction may be alkaline, neutral or acid—an absence of acid being noted in the greater number of cases.

The etiological factors mostly concerned in the production of this condition are indiscretions in diet and the abuse of alcohol, although it must be remembered that a continued action of extrinsic or intrinsic factors, as noted in *hyperchylia gastrica*, may ultimately lead to a deficiency in the secretory ability of the glands as a result of prolonged overstimulation, finally providing an *achylia gastrica*. However, accompanying this deficient acid secretion, there may be an excessive production of mucus—*gastro-myxorrhœa*—or we may get a *gastro-myxorrhœa nervosa*.

Hypersecretion is not hard to diagnose and its recognition is of great value in arriving at an ultimate diagnosis.

RETENTION (MICROSCOPIC EXAMINATION); ITS RELATION TO SPASTICITY
OR BEGINNING ORGANIC (BENIGN OR MALIGNANT) OBSTRUCTION

Too great significance cannot be attached to the microscopic examination of the fasting stomach contents. Where we have found a hypersecretion to be present, it enables us to decide whether we are dealing with an irritative lesion, and possibly associated pylorospasm—mild or severe—or a beginning organic obstruction. In the greater number of cases, this is not difficult if thorough treatment and study are carried out for a sufficient length of time; for if the hypersecretory patients are given anti-spasmodics, sedatives, proper diet and bodily rest with appropriate hygienic surroundings, they will usually get better; whereas patients with a true obstruction, after temporary improvement (which at times is marked), show a continued and progressive disturbance of motility.

*1. Microscopic findings in cases of hypersecretion and spastic
pylorus without macroscopic food retention
(gastro-succorrhea)*

Microscopic examination shows epithelial cells, free nuclei and spirals, and should the pylorospasm be intense and prolonged, a considerable number of starch particles are present. The absence of these particles should always be noted.

In *gastro-myxorrhea*, we may have the same findings except in those cases which show an absence of free acid. In these we meet with a greater number of epithelial cells, but fewer nuclei. If catarrhal or suppurative conditions of the sinuses or the upper respiratory or digestive tract are present, an excess in leucocytes will be found, owing to the fact that these cellular elements are not acted upon because of the weak digestive powers of the acid-free gastric secretion. Films of mucus, in which the various cells and debris are enmeshed, are often noted.

It is interesting and highly instructive to watch the disappearance or persistence of evidence of obstruction. A few starch particles may be seen at first but they may vanish after proper treatment. On the other hand, at the first examination there may be no starch granules, and then later a few may appear until large numbers are present;

and with these may be seen a stray muscle fiber or a few neutral fat globules. At this stage, a positive Hausmann test will probably indicate gross obstruction although it may be quite a moderate grade.

2. *Microscopic findings in cases with food retention*

Cocci and bacilli flourish in gastric juice low in free acid, whereas sarcinae and yeast grow abundantly in a secretion rich in hydrochloric acid.

a. Reaction acid (free HCl). In addition to normal findings (epithelial cells, free nuclei and spirals) we see starch granules, muscle fibers, fats (neutral as globules, or fatty acids in the form of crystals) sarcinae, yeast, indistinguishable debris, and bacteria. Such a picture speaks for an obstruction possibly of a benign origin, the organic lesion being an active ulcer with marked infiltration and edema, or an old contracting scar—benign tumor within or pressure from without. However, in all cases, we must always try to determine whether or not the lesion is malignant.

b. Reaction, neutral or alkaline. The same findings are met with except that sarcinae are absent. In these cases we should be suspicious of the transition from a benign to a malignant process.

c. Reaction acid (lactic acid present). The various elements noted in *b* are present, but in addition the Oppler-Boas bacilli are often found. Their presence is always suggestive of malignancy, although etiologically they may be met with in any condition in which marked obstruction is associated with a lack of free hydrochloric acid. Bacteriological studies thus far have been barren of diagnostic value.

VARIOUS MATERIALS WHICH MAY BE REGARDED AS EVIDENCE OF HIGH GRADE OBSTRUCTION

Experience has unquestionably proved that, after appropriate treatment, if we continue to aspirate contents consisting of carbohydrate, fat and protein, the residue of what has been eaten twelve hours or more previously, it is certain that a high grade organic obstruction exists.

The material recovered is often decomposed, putrid, and of a muddy, mushy consistence, with a sour nauseating odor. The foods are in various stages of decomposition, and a certain amount of thick, ropy mucus is present, due to the gastritis which practically always accompanies these chronic conditions. Remnants of food eaten days before are often discovered.

Occasionally, in cases of partial obstruction due usually to pylorospasm from extrinsic or intrinsic causes associated with an atonic condition of the gastric musculature, we may have, under varying conditions, an atonic dilatation with temporary complete inhibition of motor function, a clinical picture which closely simulates that of gross organic obstruction.

EVACUATION TIME; VARIABILITY

The discovery (by aspiration) that the stomach is empty twelve hours after a rice retention meal speaks against the presence of organic obstruction. However, we feel that this finding should invariably be supplemented by a thorough microscopic investigation; and furthermore, if symptoms are not relieved, shorter retention tests should be instituted.

Of course, as in all other deductions, exceptions and modifications are to be noted. In the first place, we are not in agreement with Hausmann's original statement that the finding of macroscopic starch twelve hours after a test meal always speaks for organic obstruction. We make this statement only after an extended experience with cases showing a positive Hausmann test in which, after dietetic and medicinal treatment, the patients have recovered their normal motor capacity. These may represent a class of cases in which we are dealing with pylorospasm of intrinsic or extrinsic origin. Again, in cases of ulcer an inflammatory reaction may have occurred with marked edema because of serous exudation and have led to gross retention.

But here we also may witness a return of motor powers approximating physiologic functioning after palliative measures have been instituted; and if the ulcer itself does not contract down and block off the pylorus, the motor power may be ultimately restored to normal.

The rice retention meal may be made to serve as an excellent index of the exact time of evacuation, for some patients, in whom the test for a twelve-hour retention are negative will show a delay in emptying capacity by giving residues below the twelve-hour period (i.e., after ten, eight, seven hours). This condition is met with in pylorospasm, atony or a high position of the duodenum. This method may also serve as an excellent criterion of the response to therapeutic measures.

SUMMARY

All in all, no one test will give us such valuable information as that to be obtained by a close study of the fasting stomach. In view of this fact, it is hard to understand why this most desirable and instructive method is not universally used.

CLINICAL GASTRIC ANALYSIS, WITH DETAIL OF METHOD, AND A CONSIDERATION OF THE MAXIMUM INFORMATION TO BE OBTAINED¹

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We have not endeavored to present anything particularly new in this study, but it is rather our purpose to present in detail a practical, *clinical method* of performing a fractional gastric analysis and also to re-emphasize the statements of other writers that the estimation of the acid values is the least important of the many points that can be learned from such an examination when intelligently conducted. We wish particularly to stress a few points which to us seem important, and to amplify certain microscopic observations which are helpful in arriving at a diagnosis. The method to be outlined we have found practical for both dispensary and private practice, and the information obtained has amply repaid us for the large amount of time consumed in securing detailed facts.

No two fractional charts can be compared unless they have both been done under identical conditions, and the same points noted for each, and the obvious advantages of a standard technique are seen when an attempt is being made to analyze the deviations from normal in any given chart. This is even of greater importance when two charts from this same patient are being analyzed. We also wish to emphasize the need of investigation into the associated findings of the stomach, other than the acid values. These include the presence of mucus and bile, and the addition of pathological products such as bacteria, pus, blood and tissue juices. These associated findings all have a direct influence on the interpretation of the acid curves and also yield much information as to the intra- and extra-gastric pathology.

We will not enter here into a discussion of the relative merits of fractional analysis versus the single extraction method, other than

¹ All charts and illustrations have been omitted in this article. For references to charts and illustrations as appear in this paper consult the New York Medical Journal, September 7, 1921.

to say that we agree with Best (1), who says "The advantage of these curves in their superiority over the older one sample test, is comparable to the advantage of the moving picture over a single snapshot."

It has only been since 1914 that fractional gastric analysis has been in general use. At that time Reh fuss (2) revived the fractional method and gave it a fresh impetus by using the small sized tube with metal tip. In this and subsequent papers this investigator laid down certain fundamental principles of fractional analysis to which subsequent writers have been able to add nothing of vital importance. So-called normals, as well as abnormals, were studied by Reh fuss and Hawke, Best, Rutz and others to determine a *normal* curve and institute a standard. But since the type of normal curve could not be stabilized, other investigations took place involving enzyme action of gastric and duodenal juices, together with microscopic observations of fasting and digesting stomach contents.

The fractional analysis method is simple, safe and extremely sane, and is a method not only of choice but one of necessity where gastric function is to be studied. Who of us would think of returning to the one hour test extraction after he had experienced the value of the information to be obtained by the fractional study method. It presents for your elucidation, graphically recorded if you so desire, the acid values of the contents of the stomach at any time you may care to estimate them. Errors of secretion and motility can be observed either of the fasting or digesting stomach. The time of duodenal reflex can be checked up and matched with the appearance of blood, pus, or duodenal exfoliation in the stomach; a strong confirmatory observation in suspected duodenal ulcer, if they should be coincidental. The time of mucoid impregnation of the contents can be estimated, and microscopic examination can be made of the fasting and digesting residues.

But, to turn now to the detailed description of our method of performing the actual test. Each patient is given the following type-written instructions preparatory to presenting himself for a gastric analysis:

At 9 o'clock the night before examination eat one meat sandwich (any kind of meat) with 20 raisins or 6 stewed prunes, and drink a glass of water or cambric tea. Eat or drink nothing after this, either during the night or early morning, until we give it to you in this office.

Do not brush teeth on morning of examination.

This motor meal is to be taken twelve hours before the test is to be started, the principal object of the long fast being to have the stomach empty so as to get a true picture of both the acidity and microscopy of the interdigestive stomach. The purpose in not brushing the teeth is to avoid trauma to the gums with the subsequent misinterpretation of the swallowed blood when found in the stomach. The patient is warned against swallowing post-nasal discharge and bronchial excretion during his waking state.

When the patient presents himself a small sized gastrointestinal tube with any one of the various metal tips, is passed into the stomach. Note is made of the way the patient takes the tube, whether quietly or with retching, and to what extent the gag reflex is manifested (*vagotonia* vs. *sympathetico tonia*) and evidence of cardiospasm watched for. The entire contents of the stomach should be gently lifted out and saved for subsequent examination. The patient is then instructed to place the tube on one side of the throat bringing it out into the buccal space behind the last molar, and in this position he will find that it interferes very little with his comfort in eating the test meal.

In the selection of a test meal we agree with Rehfuß (3) who says "A fixed test load, simple and accessible, readily withdrawn, and capable of showing both secretory and motor variations, as well as pathological products, is a *sine qua non*, as the basis of intelligent analysis of the stomach," and we have long used the true classical Ewald meal of 50 grams of white bread and 350 cc. of water (as personally taught by Ewald to one of us in Berlin in 1914). Approximately 50 grams of bread is represented by two $\frac{1}{2}$ -inch slices of white bread 3 by 3, with the crust cut off.

From the time of the last swallow of bread and water up until the tube is finally removed at the completion of the test, the patient is instructed to expectorate the saliva into a receptacle, the object being two-fold. First, to prevent its obscuring the analysis by mechanical interference, and by lowering the acid curve, and, second, by recording its amount, an added bit of information is obtained relative to *vagotonia* (*hyperptyalism*) and enzyme activity can be estimated.

Fifteen-minute extractions are now made over an average period of two hours, making eight extractions in all. The first seven of these are not to exceed 10 cc. each, and each amount is to be measured and recorded, but at the two-hour extraction the stomach is entirely emptied. The material from each extraction is filtered through gauze or linen, and the filter then tested for starch with iodine solution. In

this way the point at which the stomach becomes empty can readily be determined. If the stomach does empty before the two-hour period an attempt should be made to continue the extraction to the end of the test, as much additional information may thus be obtained. When the stomach is emptied at two hours it is then lavaged with 250 cc. of water to prove not only that it is empty of the fluid part of the meal, but also that it is empty of bread crumbs which may remain in dependent portions. The tube is then removed.

This portion of the test being completed the collected material is examined immediately, if possible. This point is of importance, since evaporation of the samples increases their acidity, and the continuation of digestion changes the relation of free and combined hydrochloric acid. Each sample is examined grossly for amount, chyme, mucus and bile, and chemically for free hydrochloric acid, total acid and occult blood. The fasting stomach content should always be examined microscopically. In testing for acid 1 cc. of filtrate is titrated against 1/100 sodium hydroxide, of which the number of cubic centimeters is multiplied by 10 giving the degrees of acidity per 100 cc. gastric contents. Dimethyldiamidoazobenzol and phenosulphophthalein are used as indicators. In testing for occult blood either a freshly prepared solution of benzidine or the commercial occult blood tablets are to be used. Rutz (4) has shown that hematin granules have a tendency to adhere to other particles in solution and that, therefore, the sediment gives a more delicate reaction.

With the figures obtained from the titrations a graphic chart of the changes in acidity is constructed, using the degrees of acidity as ordinate and time as abscissa, and making thirty minutes the equivalent of 30°. The total amount of material withdrawn is computed and this is subtracted from the 350 cc. originally given, and therefore the amount that has passed the pylorus can be noted and a clinical estimation of gastric motility is thus obtained.

We wish here to refer to a further procedure that was first advanced by one of us (Lyon) in 1915 of obtaining the contents of the stomach crypts. The mouth and throat are rinsed with an astringent mouth wash (liq. zinci formaldehyde) followed by a 1-grain-to-the-ounce aqueous solution of potassium permanganate, and this in turn washed with sterile water. The sterile tube is then introduced, and the fasting residuum aspirated and the stomach is washed with 250 cc. of sterile water at body temperature run in the tube through a glass container elevated about 2 feet above the patient's mouth, and im-

mediately siphoned to a 250 cc. graduate on the floor. The inflow and outflow durations are recorded, inasmuch as we feel that this gives us certain clinical data relative to state of tonicity of the gastric wall. Repeated washing is done until the return be crystal clear, and unless there be marked gross retention this is usually accomplished in from two to three washings. Then a weak solution of zinc chloride and formalin, 250 cc., is run in and allowed to remain for one minute, when it is siphoned off. This acts as an astringent and causes the mucous membrane to contract, and the secretions in the duct are forced out and appear as floccules in the subsequent washings. These floccules are pipetted out of the solution and examined microscopically, or the complete sediment may be collected and run through a hardening process, mounted in celloidin and sectioned and stained and examined by microscope, just as any pathologic specimen is handled. The technique of the method (5) was presented in 1915 and has proved of great help to us in keeping permanent records of intra-gastric pathology.

THEORETICAL DISCUSSION

Gastric analysis is primarily a measure of gastric work, fasting and digesting, motor and secretory, as has been pointed out by Rehfuess and Hawk (6), and in order to measure this work done and compare it with a normal, a standard test load must be given the stomach to handle. This measure of work is in reality the measure of the physiological function of the stomach, secretory and motor, and any deviation from the normal in either acid values or motor activity must be viewed only in the light of pathological physiology. But gastric analysis when intelligently conducted is more than just a measure of the work done, it is an indicator of true intra-gastric pathology. The evidence of such pathology, however, lies in the addition to the gastric juice of the products of that pathology. These are mucus, exfoliated epithelial elements, pus, blood and bacterial colonies. And there is a third and equally important side to gastric analysis for it serves as an indicator of extra-gastric pathology. It has long been recognized that most systemic conditions, and many strictly local conditions, even though far removed from the stomach, may influence that viscus. The evidence of such influence is seen indirectly in its effect on the acid curves, and directly by the finding of products of this extra-gastric pathology added to the gastric secretions. Examples of this latter are the findings of swallowed pus and the occurrence of occult

blood associated with biliary regurgitation which, according to Reh-fuss (7), is the only direct evidence of duodenal ulcer to be obtained from a gastric analysis. To this should be added the findings of regurgitated duodenal epithelium, pus, mucus, and bacteria.

Whenever there is any deviation from the normal values in a given gastric analysis it is of the utmost importance from the clinician's standpoint to determine whether these variations are due to intra-gastric pathology, or are the indirect evidence of conditions outside the stomach. But before the deviations from normal can be appreciated it is necessary that we have some conception of what constitutes normal findings in a test conducted as outlined above. We will, therefore, briefly discuss what we consider as "normal" findings as found in patients who have not only no gastrointestinal ailments, but are also free from any general or other local conditions. We will also point out the chief types of pathological curves.

To consider first the twelve-hour fasting stomach contents. The amount varies in health from a few cubic centimeters to 50 to 80 cc., anything above that amount being due either to hypersecretion or retention, that question being decided by the microscopic picture. Sediment up to 5 per cent of the total amount recovered cannot be considered beyond normal limits. Mucus that floats is generally freshly swallowed, whereas the type of very viscid stringy, intimately mixed mucus is usually associated with absence of free hydrochloric acid at that particular period of the gastric cycle.

The acids values of the fasting stomach we have found to vary within wide limits. Attention has been called by different writers to the "fast" and "slow" normal stomachs, and we feel that there should be a comparable secretory classification of "high" and "low" stomachs both within normal limits. It would seem that this question of "fast" and "slow," "high" and "low" is often dependent on the *habitus* of the individual, and that this fact must be kept in mind. This accounts for the variations in the acid values between persons, but we have found that if the stomach contents of the same individual be examined daily under the same conditions of time, and length of preceding fast, the greatest variations of acid values will frequently be found. The explanation of this is, we believe, that the level of acidity in the inter-digestive stomach is an expression of a vital function, and like other vital functions it fluctuates from day to day and is easily influenced by such things as loss of sleep, worry, nervousness, etc.

The question of biliary regurgitation is one to which we have given considerable attention. We believe that frank macroscopic regurgitation of bile into either the fasting or digesting stomach is, with certain exceptions, an abnormal finding, one which points to disturbed physiology of the pylorus and duodeno-biliary zone. The exceptions to this statement are, first, if the patient does not take the tube well, but gags and coughs, bile may be squeezed out of the gall tract by the simultaneous contraction of the abdominal muscles and the diaphragm, and be regurgitated into the stomach. Second, in those cases of marked hyperacidity, alkaline duodenal contents mixed with bile may be regurgitated into the stomach in an effort to physiologically lower the excessive acid. We have been led to make this statement by the following facts: In healthy individuals the duodenum in the fasting state is bile free. The normal direction of progression of the contents of this portion of the gastrointestinal tract is aboral—there is no reversed peristalsis. Interference with the innervation of this portion of the gut by operative procedure, excision of duodenal ulcer, cholecystostomy and cholecystectomy increased the percentage of biliary regurgitation. Post-operative cases showed a larger percentage of biliary regurgitation than non-operative cases, and those showing evidence of pathology in the upper right quadrant showed a higher percentage than those in whom no pathology could be demonstrated. Most of the writers on this subject have stated that bile in the stomach is a normal finding, being present in about 50 per cent of the cases, but in a series of gastric analysis on patients with gastrointestinal complaints we found fasting regurgitation in 36 per cent, and digesting regurgitation in 23 per cent. Jarno (8) found that there was a regurgitation of bile into the fasting stomach in association with the normal hunger contractions, and this may account for the finding of bile in normal stomachs.

The microscopic examination of the fasting stomach contents is of the greatest importance, in fact we attach as much importance to it as to the motor-secretory curve in determining gastric pathology. The whole question of the interpretation of the microscopic picture seen is one of relative values, for prolonged search will find examples of all the types of cellular elements. As was said above, sediment up to 5 per cent of the amount extracted may be considered within normal limits, but anything above this must be looked upon as pathologic, and its source must be fixed. Swallowed mucus either floats, or is seen in dense brownish masses, while duodenal mucus is usually

associated with biliary regurgitation. Gastric mucus seen grossly is generally flocculent. All these types may be seen in the same sediment, and if so each must be examined and the relative amounts noted.

In making a preparation for microscopic examination a small amount of the material is placed on a slide and a cover-slip dropped on top. On looking at this with the high power objective it will be seen that either the cells are practically intact or that the cytoplasm is entirely digested away, leaving only the more resistant nuclei. The nuclear remains of gastric cells are oval, highly refractive bodies, and the polymorphonuclear cells are seen as groups of two or three small globules. There are always a certain number of leucocytic cells in the fasting stomach, but if these occur in sufficient numbers to constitute pus, they are a distinctly pathological factor. The type of epithelium with which the pus is associated, is the deciding factor in locating the point of its discharge and the finding of a predominance of buccal or respiratory epithelium should lead to a careful search of the mouth and respiratory tract for evidence of infection. In an acid stomach both the chief and parietal types of gastric epithelium can be seen, but it must be remembered that these, as well as other cells, are dead or dying, and all show cloudy swelling.

In regurgitation from the duodenum the cytology is usually well preserved. Duodenal cells, round, cuboidal or oval cells somewhat longer than pus cells, can be recognized, and at times bile stained columnar epithelium from the biliary tract can be seen. Bile stained pus cells, when found in association with this latter type of epithelium, point to infection somewhere in the duodenal-biliary tract. When bile is regurgitated into a stomach containing free HCl the bile salts are precipitated, giving the material grossly a turbid appearance, and microscopically appearing as small clumps and masses of yellow amorphous material. When the regurgitation takes place into an acid stomach there is no such precipitation. Bile that has been resident in the stomach for some time assumes various shades of blue and green.

Normally there is no gross or microscopic evidence of food retention in the twelve-hour fasting stomach. Retention when found is not pathognomonic of any one pathological process, but it is frequently enough associated with graver conditions in and about the pylorus to necessitate a careful investigation into the causative factor.

The question of the bacterial flora of the stomach is one on which much still remains to be written. Bacterial bodies can always be found in the stomach, but whether they be living organisms, and whether they be truly resident in the stomach, constituting an infected gastritis, or only bacteria in transit, are points of vital importance to determine. To answer the second question first, bacteria that are in transit are seen as single organisms or grouped in small masses. If, however, viable organisms linger long enough to become implanted in the gastric mucosa they grow in colony formation just as colonies grow on the surface of any suitable media. When they become detached and are seen in the fasting stomach contents they are entirely similar to the surface colonies on a Petri dish when viewed through a low power ocular. The final answer to the question of viability must depend on culturation, but we feel that for all practical purposes the finding of *colonies* associated with gastric mucus or epithelium is positive proof of the presence of infection in the gastric mucosa.

To the finding of occult blood in the *fasting* contents we do not attach much importance unless the guaiac reaction be very strong. This is because in spite of the precautions taken, it is generally extra-gastric in origin. It is only definitely of value when the naso-pharyngeal and bronchial secretions have been proved to give negative reactions.

Having completed the examination of the fasting stomach content, the next point in the examination is the analysis of the type of curve obtained. We agree with Best, who says, "The actual acid value means very little. The shape of the curve means more," and with Rehfuess (9) who says, "There is no pathognomonic curve in any gastric condition," and yet we feel very strongly that there are certain types of curves that point to certain conditions. From a study of many analyses we find that they all fall into one of five groups. Any of these groups, with the exception of the third, can be associated with either hyperacidity or subacidity. The question of the amount of acid secreted in response to the stimulation of the test meal seems to us to depend on the irritability of the vagus, and the state of fatigue of the gastric glandulature.

Type 1. "Normal" curve. This is the type of curve in which the apex is reached in from sixty to seventy-five minutes, and a return to within 15° of the fasting values occurs at one hundred and twenty minutes. It is the type of curve seen in perfectly healthy persons

and also in certain early states of intragastric conditions—principally catarrhal. The points indicative of an early catarrhal process are gastric muco-pus in the fasting stomach content, and mucus and blood in the digesting stomach.

Type 2. "Extra-gastric" curve. In this type the curve rises steadily during the entire two-hour period, or until the stomach becomes empty if there is an associated hypermotility. This is the type of curve that is due to reflex irritation from pathology outside the stomach. It is seen in cases of duodenitis, duodenal ulcer, gall bladder conditions, appendicitis and sigmoiditis. It may be found in association with a "clean" stomach or with all the evidence of a high grade infected gastritis, but in either case the principal source of trouble is extra-gastric.

Type 3. "Achyilia." This is a type of curve in which there is no free hydrochloric acid present at any time. It is most frequently seen in cases of malignancy of the stomach in the later stages, in oral sepsis, long standing cholelithiasis, and in the severe anemias, either primary or secondary.

Type 4. "Step-ladder" curve. In this type of curve the smooth ascent is broken by drops in both free hydrochloric and total acid, unassociated with biliary regurgitation, followed by a rise to a still higher level than preceding the drop. This curve is not often seen, but is of grave significance. We have only seen it in ulcer cases in the active stages, and it is generally preceded or followed by hemorrhage. Best illustrates a curve of this type, and notes that there was a recent hemorrhage.

Type 5. "Delayed digestion" curve. In this curve there is a primary small rise followed by a drop, and then by a practically normal curve. In certain cases of this type the free hydrochloric acid does not come in until the secondary rise, and it corresponds to the psychical achylia of some writers. A possible explanation of this type of curve is that the primary rise represents the psychic secretion, and the secondary rise the hormonal secretion. This latter, which should normally pick up and carry on the psychic secretion, is delayed, and therefore permits of a wearing off of the psychic stimulus and a consequent drop in the acid values.

In addition to the study of the fasting stomach content, and an analysis of the type of curve, there are certain other findings which must be tabulated. The motor element is of great importance, and carried out as detailed earlier in this paper, we believe that it gives a

more accurate estimate of gastric motility than the X-ray examination for six-hour barium retention. In all cases of achylia there are certain associated tests that should be done. They are the tests for pepsinogen and lactic acid, and the Wolff-Junghans reaction. The details of these reactions do not fall within the scope of this paper, but can be found in any standard work on the stomach.

Mucus, when found in all the extractions, especially when associated with low salivary output, is probably swallowed; whereas, mucus, appearing only in the second half of the examination, is generally gastric in origin. The interpretation of bile in the digesting stomach has been discussed above and need not be repeated here. The finding of blood in the digesting stomach must not be taken as evidence of ulcer or neoplasm unless the evidence of careful history and physical examinations lend their support to such a diagnosis. Rather, it is to be interpreted as congestion with diapedesis or miliary erosions, and should lead to a careful examination of heart, lungs and liver.

In closing we want to say a word about the diagnostic and prognostic value of repeated fractional gastric analyses. We have found this method of checking up our findings of the greatest practical value. It is especially useful in cases where repeated X-ray examinations cannot be obtained, giving not only a very accurate picture of the motility of the stomach, but also adding the secretory curve. It has also been of value in following the progress of medical treatment, and in estimating the benefit derived from surgical interference. In many cases, with complete arrest of symptoms, it will be found that the fractional analysis has not returned to normal, and unless treatment is continued a relapse is quite likely.

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DISCUSSION

DR. THOMAS R. BROWN, Baltimore: I might say that Dr. Gaither's paper represents the real summation of the results at our Clinic at Johns Hopkins for eight years. We started the clinic eight years ago, having come from Germany, and became imbued with the value of the fasting stomach test, and it has been a routine in our clinic from that time. I think both papers show the value of that beyond question. I think with regard to the functional method Dr. Lyon has said that we are throwing a monkey wrench into the machinery of progress; I think after all, the question is, Do the methods justify their use? I think the fact that many admit that the least we get is the acid readings, is a fundamental argument against its use, and if you have three to five normals, I challenge anyone to absolutely elucidate the individual curve and to get a definite fact out of it. It is pyrotechnic, every paper is filled with curves and charts, but if it does not help in treatment or diagnosis, I can see no indication for it from the clinical side, even though it may be of value from the point of view of clinical pathology; but even then it cannot be fundamentally sound because any method in which a foreign body is introduced produces at once an unphysiological factor. We, when this method came out, studied and used it just conscientiously as anybody else, but finally had to admit that it did not teach us anything essentially different from the knowledge obtained from the simpler method. There are too many variable factors, and you cannot draw different conclusions when you have so many variables to deal with. And so we are content to depend upon the rough secretory findings as obtained by Ewald's procedure plus the fasting stomach test. After all, those who go back in medical history will remember that there is no fundamental difference between this method and the methods employed in 1880 by Hayem and others in Paris, and again practically all of the men who tried it came to the conclusion that it did not give enough additional information to warrant its use, and that, after all, is the test of the value of the method. The danger of it is that we get dependent on a relatively complicated measure, and we forget the far more fundamental things. After all, the practice of medicine is never the study of one test, and the great danger of this method is that it makes us forget the far more fundamental things such as history taking and the real interpretation and interrelation of the disease processes in the body and the fact that in the vast majority of cases the picture is so varying that if I had to abandon one method, it would be the abandonment of the test meal method every time. Perhaps we are old fashioned, but after all the only safe digestive man is the man who has been the broadest clinician in the broadest sense of the word, who only uses tests after he has asked himself if they have helped him. If they help, they should be retained. But it seems to me that the man who bases gastric pathology on secretory findings is leaning upon an exceedingly fragile reed.

DR. FRANK SMITHIES, Chicago: I think that it takes a brave sort of fellow as Dr. Gaither really has shown to read a paper like his and to say that in *not using* the fractional method of gastric analysis we are really "down to date." But at the same time, I believe that there is a middle ground in these clinical opinions. Coming over the hill with Bryant, I noticed men were excavating with a steam shovel. The steam shovel dug out the free-way, and then men were set to dig out the little ditches and corners; similarly, it is very likely that the procedure which we have

adopted in our clinic, for some time, might be used, namely, the particularization of the study of the case to the individual; we secure our information in the light of the clinical history, general physical examination and laboratory analysis and we emphasize the information secured from the fasting stomach. Should the case prove unusual, from the secretory or motor angles, then we make observations in regard to the digestive cycle by fractional analyses. Frequently such study really adds nothing of particular value to the management of the patient—though at times I am sure that our therapeutics has been changed to the patient's benefit, by altering its type or time accordingly as we have learned of anomalies in the digestive cycle by fractional studies.

Some time ago I published a paper (American Journal Medical Society) detailing test-meal findings in more than 7000 individuals, and in it summarized what value test meals had in the elucidation of gastric upsets. I have not changed my opinions a bit from those expressed in that paper; perhaps I have gotten sclerosis, but there seems to me to be certain fundamentals in that paper, which the number of cases studied demonstrated and which such a great material rendered useful because the very mass of the work on a uniform principle of action eliminated confusing errors such as might occur when only a few cases are studied. But a man must get acquainted with the tools with which he is working if he is going to diagnose the ailments of his patients; very likely the man who is living in the atmosphere of the Rehfuß tube is able to do that as well as the man who is living in the "garden hose" atmosphere; he learns properly to interpret his findings in conjunction with his other examinations of the given case.

With regard to fasting stomach residues: frequent examinations of the same stomach will reveal striking and important differences. I would like to emphasize strongly the necessity for the microscopic examination of what is secured from fasting stomachs; such information is frequently of more worth than are estimations of chemical activity. Further, we must not forget this physiologic fact—during the day the stomach is at work and is not resting and undergoing processes of repair; during the night there is a period of gastric rest and physiologic repair which varies for the individual at different times and for groups of patients similarly affected—epithelial exfoliation, mucoid degeneration, bacterial discharge, collection and growth occur in a stomach at its "resting" stage and with a low mobility rate. Many "fasting stomach" pictures, microscopically studied, represent only normal gastric degeneration and repair complicated by the mucus and bacteria, etc., which are swallowed during rest. During the night there is a period of repair comparable to that which takes place in the skin; one need only compare and contrast the findings from the same individual studied at different times to appreciate these facts.

Coming back to where we started, it would seem to me that there is a midground. The study of the individual is the thing, and he should be studied, not once but many times by the same routine. The observations on the case shown this morning by Dr. Stockton were valuable as demonstrating just what might happen in one individual if one did nothing for him but merely observed him over a long period of events. There is a basis for both of the procedures suggested by Lyon and by Gaither, but they must be employed intelligently, and with more discrimination than is implied by "routine" methods in hospitals, clinics and private practice. If we do not so employ them, neither of them are worth the time it takes to carry them out.

DR. HORACE W. SOFER, St. Louis: I wish to call attention to an article in the Archives of Internal Medicine by Dr. Frank D. Gorham of St. Louis, Missouri.

Dr. Gorham got practically the same secretory curve by means of rapid successive extractions of stomach contents that he got in the usual fifteen-minute fractional method. This demonstrated that a single specimen secured at a given time was not indicative of the acidity or secretory response of the stomach at that time.

DR. MAX EINHORN, New York: I have been very much interested in the two papers and I am glad that both gentlemen agree that the examination of the fasting stomach is of value; and I would like to lay more stress on that. I think if the tube has done anything else than to examine the patient in the fasting condition to see whether the stomach is empty or not, is alone of the greatest value in clinical medicine; because there are a great many diseases which cannot be discovered except when we do that, and those are the cases of pyloric obstruction; and here I want to say that it is not of so much importance whether there is fluid or not, but the important thing is to microscopically look at it, and if you see that you have bread or rice or spinach from the day before, then you have to deal with a serious condition which requires attention, but if you find fluid and no food at all, then the microscopic examination is still of value. And I am always disappointed when the nurses write down, "fasting stomach—found 60 cc. of fluid, dirty looking" or something like that. You cannot make out anything from that, but if you say there is food in it, potatoes, raisins, etc., then you can make something out of it, whether there is food in the stomach or not. This is of greater importance than the examination with barium six hours later because here we do not exactly—the stomach should be empty—but the importance of the residue with barium is not to be compared to the finding of a fasting stomach which contains food that does not belong there, and we know that is a pathological entity.

DR. GEO. R. SATTERLEE, New York City: I believe Dr. Lyon has struck the keynote in studying the gastric pathology in separating the intra- and extra-gastric infections. Now something is the fact in gastric lesions. I believe that the studies of Dr. Rehfuess have been extremely valuable and should be used. I believe that the fractional gastric analysis has come to stay. I think that what we learn about the physiology of the stomach is of no diagnostic importance. But the other side of it is the study of the microscopic contents and the bacteriology.

Now in the work we have been doing along this line we have found that by the duodenal tube, getting the contents from the stomach and duodenum, that a great many cases of infection have been cleared up by means of a study of these bacteria; and by vaccines. Here, for illustration, is a patient who has had the gall bladder removed and she had no improvement in her original symptom which was pain in her right upper quadrant. When she first came in we tried duodenal lavage and got a large amount of pus filled with streptococci from the duodenum, and we tried lavage of the duodenum with magnesium sulphate and then we had a vaccine made up of streptococci and gave that with excellent results so that her pain and general condition cleared up.

Now if we find bacteria in the gastric contents or in the duodenal contents, they are either inherent in there or else they come from some other place, from the swab,

for instance, from the mouth; so I think under those conditions it is certainly well to look into the origin of that infection, and we hope to get next year some of the work on gastrointestinal lesions from the study of the infections of the mouth, teeth and tonsils and the effects of treatment along those lines. We have found in a general way that a good many cases of abdominal lesions such as cholecystitis, infection of the gall-bladder and also pathology in the abdomen have been so mitigated by treatment along the line of infection that operative procedures which were apparently indicated have been put off, and in another direction a good many post-operative cases which were apparent failures have been improved by clearing up these extra-gastric infections such as those in the mouth by vaccines obtained in the cultural method from these fractional methods, and I am sure you cannot have too complete a study on these cases.

DR. C. R. JONES, Pittsburgh, Pa.: No one has been more interested in these papers than I. I was also interested to hear Dr. Soper call attention to the work of Dr. Gorham. For some time I have been doing what I might call fractional analysis by giving four test meals of shredded wheat on four succeeding days, taking the entire contents of the stomach at twenty minutes on the first day, and at forty and sixty and eighty minutes, taking the contents with the Ewald tube and removing the entire contents. The reference to this subject in Pawlow's work in which he speaks of the stomach contents not being a homogeneous mass, and we are likely to withdraw from the stomach with a small tube a fraction which does not represent the content of the stomach at that time. I have done some work in distributing the contents in different beakers and in some instances I have had as much variation as 50 points in the total acidity of the gastric contents removed at the same time through the Ewald tube.

DR. MARTIN E. REHFUSS, Philadelphia: This discussion is elucidating, and I cannot help realizing that this one thing is true that the indictment that any one of us relying on any one method is equally against any one. I am in favor of any method of any one that can help the individual who is sick, and when it comes to gastric work, the medical man if he has freedom removed from himself, is removed from progress. That means this—I have spent not one but a number of years, I have watched this thing and studied this thing. We have been disappointed in this thing. I believe that a thing is not pathognomonic of gastric ulcer and no symptom pathognomonic to occur, and there is not one but many things of fractional analysis as shown that I cannot explain but that demands solution. Fractional analysis, I introduced that word, I mentioned the fifteen-minute phase, the idea of a man who took the fifteen-minute curve and said that he should make it fourteen-minutes and sixty seconds was not imbued with the fact that gastric digestion is a changing phenomenon. If the stomach was a rigid tube, it might be well and good but the instant you introduce something into the stomach, the stomach reacts, and the study is not the study of the secretory phases or of the acidity but every single specimen by fractional analysis can be submitted to the study of the bacterial examination and of the albumin content, etc., and to the study of the psychological examination, and this is the idea of investigating the stomach. If you investigate at different phases, you will get different results. If I do it at one fractional interval, I might get one thing and another man get another. A persistent finding like an X-ray spasm is an important thing to find.

Fractional gastric analysis has three functions: it measures secretory function, and it measures motor function and it estimates the age of the gastric function, and those three facts can be determined in any way you like. If you want to study it in an empty stomach all right; or after any phase. Now we found in our cases of normal individuals that we never found food in the stomach after six hours. So we are sure that food after six hours is evidence of pathology. No normal individual with any type of food showed anything in his stomach after six hours, and yet you will find many of these patients showing food after six hours. I do not mention this because I do not agree with both these gentlemen. I think, however, that Dr. Lyon has hit the thing on the head in saying that this is not an estimation of the acidity; it is an estimation of all the things you can throw light on in the estimation of gastric disease. It is not only the estimations of cancer, but it is the estimation of two hundred fifty varieties of things in the stomach that bring about gastric changes. I emphasize this because I do not believe that there is anybody today who can pass judgment on this particular method of examination, and until I know more, I am going to continue to use it.

DR. B. B. VINCENT LYON, Philadelphia: I would like to say one word about this—I think it is a very gratifying thing that we can consider this association as an open forum and that we can freely discuss various methods of procedure without, I am sure, any feelings of personal antagonism entering into it.

I was very much interested in Dr. Gaither's paper, but I am frankly a little bit disappointed to see a monkey wrench thrown into the machinery of progress. I believe unquestionably that the fractional method of analysis of gastric function is a method destined to remain among all of us who are anxious to get at the truth of the matter. I do not see any comparison of the information that can be obtained by single test meal extracts with that obtained by longer continued or fractional studies. I am absolutely in agreement with Dr. Gaither, however, that the least important merit of the fractional method of analysis is the determination of the acidity values because they are a little too confusing in their interpretation, but I feel that the associated help that we get from the examination of other products of gastric digestion primarily other than of secretion, is the thing we want to hang on to in gastric analysis.

Dr. Bartle has asked me to close the discussion on our paper and that of Dr. Gaither. I think we have had a very interesting afternoon. It seems to me on listening to the discussion that it emphatically proves that the interest in gastroenterology has increased. I do not believe there is any other study that is more important for the making of a comprehensive diagnosis than modern gastroenterology because in it are found all the necessities for clinical investigation which stimulates the proper clinical mind. I am, however, extremely sorry to see the attempt made this afternoon to sweepingly wipe away the years of effort that Dr. Rehfuß and Dr. Hawk have spent in a perfectly earnest and intelligently conducted study of gastric function. Much of his work is good, and will remain useful in differentiating diagnoses.

The point I wish to emphasize, however, is that no gastrointestinal diagnosis can be made. I agree with Dr. Brown in this as implicitly as I can—that no diagnosis can be made without the closest study of the case from every angle and it is absurd for anyone to assume that because one continues to use fractional

gastric analysis that it is used to the exclusion of all other methods. In my office we take fifteen hours of study of each new case before I am willing to pass a final opinion on that case—five periods of three hours each, one of which is devoted to fractional analysis. Certain cases take even longer. I believe that fractional analysis is going to live among the doctors who are interested to see it survive. I believe with Dr. Brown and Dr. Gaither that the least important of the three points that Dr. Reh fuss has shown—the least important in the way of derivable information, is the secretory side, but I believe the fractional method of recording gastric function is the best method we now have, because it records the secretory and motor states and gives a determination of gastric microscopic pathology. You cannot afford to limit yourself to a single examination to obtain that information.

There is a fourth point, too, in Dr. Reh fuss' platform, and that is the importance of obtaining a determination of extragastric pathology from gastric examinations; that is, the extragastric microscopic pathology may be derivable from above the stomach, the gums, the tonsils, etc., are all determinable by matching up with your microscopic gastric findings, and similarly from below the stomach the reflux from the duodenum which brings up the cytological and bacteriological evidence from diseased states of the duodenum or gall tract. I do not see how it can be ignored.

Dr. Smithies has brought out a good point, and that is the importance of frequent reexaminations. His remark about the fasting residuum is one of the most important points made today. If we did not want to get a clear conception of the diagnosis of our patients, all of us would be happy to throw over the tedious fractional analysis and not burden ourselves with useless diagnostic tasks. It is, therefore, perfectly reasonable to believe that the doctor who finds no value in the fractional examinations would do better by applying the time in other directions, but for myself I shall continue to use the fractional method of gastric analysis not so much for the secretory side of it but for the microscopic pictures that are constantly appearing—the motility rate, the reverse peristalsis, and so on, which are of great diagnostic help to me personally.

DR. JULIUS FRIEDENWALD, Baltimore: I have been much interested in the two papers and have done considerable work in the line of fractional analysis and have been greatly impressed with the results.

As to the question of increase in acidity due to the stimulation of the Reh fuss tube itself, I am convinced that this does not occur for I have made tests of the secretion of the stomach with the Ewald tube at varying periods and have found that the acidity was about the same at each period as that obtained with the Reh fuss tube.

Again regarding the variations in acidity with the Reh fuss tube, this can easily be overcome by producing a mixture of the gastric secretion. If one utilizes a large syringe a thorough mixture can be obtained of the entire gastric contents.

DR. GAITHER: After listening to the views of the various members I feel more convinced than ever of the security of our attitude, relative to the far greater value of the information gained by a close study of the fasting stomach in digestive disease than that knowledge obtained by secretory investigation.

THE NON-RECURRENCE OF GASTRIC CANCER AFTER OPERATION

SEYMOUR BASCH

New York City

In 1 out of every 3 men and in 1 out of every 5 women who contract cancer, the stomach is the organ attacked. All other methods of treating gastric neoplasms having proved futile, our only hope of prolonging life and effecting cure is in surgery. However, despite the numerous reports of radical cures that have appeared in the literature, great skepticism exists among the profession as well as among the laity as to the usefulness of operative procedures in this condition. Most of the publications inspire little confidence because they deal only with large statistical groups and vague generalizations, without presenting individual cases for critical study. Moreover, important details are usually missing. How many patients after a period of years are not only alive but also cancer-free? Do not many or all of them finally succumb to malignancy? In the favorable cases, how was the original diagnosis of gastric cancer established—clinically, chemically, radiologically or surgically? Was it subsequently sustained histologically? Nor is a bare statement that microscopic examination showed cancerous tissue altogether convincing when the name of the pathologist who made it is either not given at all or his competency is doubtful. As Dr. Stockton (1) says: "Occasionally there is a case in which the result of early excision has been so flattering that the skeptical look suspicious at the microscopic section by means of which the disease was verified."

Nevertheless, there are a number of publications from eminent sources which prove beyond all doubt that gastric cancer is curable by early operation. Thus William J. Mayo (2) in a series of 651 resections of the stomach from 1897 to 1917, in which the malignancy of the tumor was in each case histologically demonstrated, reports the following encouraging figures: Out of 311 traced, 120 patients were alive more than five years after operation: 35 lived more than six years, 27 more than seven years, 18 more than eight years, 10 more than nine years, 7 more than ten years, 5 more than eleven years, 3 more than twelve years, and 1 more than fifteen years.

Weil (3) reports the following end results from radical treatment of gastric cancer histologically confirmed at the Breslau surgical clinic between 1891 and 1911: One well after twenty-one years; 1 well after nineteen years; 3 after fourteen years, 2 after thirteen years; 1 after eleven years, and 13 well from four to nine years after operation. John Douglas (4) reports 3 cases well more than five years after pylorotomy. Peck (5) finds that radical excision was performed in 33 out of 527 cases admitted to several New York hospitals in the last six years; only 23 recovered from operation, and of these 8 were known to be well for four years or less. Woolsey (6) has 2 cases out of 18 well more than four years, and Willy Meyer (7) 1 case well more than ten years. Friedenwald (8) did not see a single recovery in 266 of his own radically treated cases, but Hartmann (9) has 3 well after five years, 3 after six years, 2 after seven years, and 1 after thirteen years. Moeller (10) reports survival for more than five years of 10 per cent of the 147 patients operated at Lund since 1898. Deaver (11) says that the combined statistics of the large clinics indicate that 20 to 30 per cent of all patients will live more than three years after gastrectomy and that from 10 to 20 per cent will be alive at the end of the five-year period.

The variation in these figures is doubtless due to the relative earliness of the operation. All writers insist upon early operation, but there are few attempts to define the factors upon which the earliest possible diagnosis can be formed. William J. Mayo (12) says that a probable diagnosis in early cancer can be established by simple methods. He seems to me, however, to be too modest in his demands upon the diagnostician. Although the mechanical and chemical signs which he enumerates may be present in some cases of very early involvement of the pylorus, they are usually only manifest when the cancer has already become well established. To advise operation in a sweeping generalization, as he appears to do, only upon the finding of a palpable tumor, obstruction, food remnants, deformities or muscular deficiencies revealed by the X-ray, Boas-Oppler bacilli, and other typical signs of cancer, certainly invites tardiness. To wait until we know positively that we have carcinoma may occasionally prevent an unnecessary operation, but, on the other hand, it works havoc on the side of sacrificing possible salvage. The surgeon will then generally find a hopeless state of affairs because of extensive metastases, adhesions to inoperable organs, the patient's inability to stand the shock, and other unfavorable factors. In any event the

prognosis is of course dependent upon the variety, situation and extent of the cancer, but as the only alternative is a mortality of 100 per cent, the patient has everything to gain and nothing to lose by prompt operation. Success is obviously directly proportionate to the earliness of the operation. Reasonable grounds for the suspicion of malignancy in these cases imperatively call for surgery, and these grounds are, in the first place, to be sought in a careful study of the history.

From the purely clinical point of view, we encounter, broadly speaking, 2 types of primary gastric cancer—1 which suddenly appears in a previously entirely well stomach, like a bolt from the blue sky, and 1 which develops on the basis of a preexisting ulcer. In the cancer without previous lesion, the growth of the tumor is much faster and the local as well as the systemic changes correspondingly more rapid. Radical therapy is, of course, more promising in the post-ulcerous form of cancer, because there is less carcinomatous tissue to eradicate and less diffuse infiltration of the stomach wall, and because, owing to the intimate association of the ulcer, the operation amounts practically only to a wide removal of the ulcerous area and of any easily excised enlarged glands.

Since the responsibility rests upon the physician, our attitude must be one of watchful readiness. No condition in medicine makes a greater tax upon diagnostic intuition and is less susceptible to hard and fast rules. When a patient in the cancer age presents himself with a gastric complaint, every clue that either tends to exclude malignancy or to a point toward it must be painstakingly collected and analyzed. Briefly reviewed, the available data are the clinical history and the chemical and radiologic findings.

1. The clinical history.

In post-ulcer cases a perceptible change from periodicity to constancy of symptoms in a person within the cancer age, should arouse attention. Though the patient may not know that he has had an ulcer, he will, on careful questioning give a history of chronic and periodic ulcer characterized by repetition of the gastric symptoms, especially periodic burning, sour belching and digestive distress, with intervals of keen appetite and marked improvement or even of entire well being between the attacks. He may even be able to recall one or more occasions upon which, for no apparent reason, he had an attack of weakness with tachycardia or even syncope—phenomena

suggestive of a hemorrhage from a gastric ulcer. Now he is conscious of stomach symptoms during the entire twenty-four hours, and they are not so closely associated with the ingestion of food as in ulcer; in other words, the ulcer symptoms still predominate, but a counterpoint of cancer is barely becoming noticeable. There is increasing aversion to food, particularly to meat. His physical appearances usually indicates decline in health, and there has of late been progressive loss of weight and vigor.

In the type without previous ulcer history, i.e., presenting the appearance of a sudden or acute insidious gastric complaint in a subject who has always been well, the onset of the trouble is usually ascribed by him to some dietary indiscretion or to a more or less improbable cause. Here there is the same gradually increasing anorexia, and especially aversion to meat, the same dyspeptic symptoms of pressure of gas, belching, even pain not necessarily connected with the ingestion of food, progressive nausea, and the same story of recent physical failing. Occasionally vomiting occurs, even in the earliest stages, sometimes associated with visible blood streaks. The appearance of this blood is what usually causes the patient to seek medical advice. A sudden gastric complaint in the cancer years with no real cause to account for its onset, which does not readily yield to the customary treatment, with the patient becoming worse rather than better, and in which palpation reveals local tenderness or the signs of infiltration or induration of the stomach or possibly a movable tumor, constitutes perhaps the earliest possible clinical picture of a primary carcinoma. This applies more particularly to growths in the body of the stomach; in those at or near the orifices we have, in addition, spasms as well as signs of obstruction. The possibility of a sarcoma, a benign tumor, or of syphilis should also be borne in mind.

2. Chemically

Since a simple ulcer calls for a high hydrochloric acid figure, gradual diminution in the amount of this acid in a middle-aged individual is an important sign, especially when accompanied by mucus and blood and a positive Wolff-Junghann's reaction. At the Mayo Clinic it was noted that the cancerous stomach always contained some acid, although free hydrochloric acid was often absent. There may be occult blood in the stool very early in the disease. In the primary form of cancer the laboratory indications of malignancy are to be found very early, while in neoplasms following ulcer, the laboratory findings very often are only those of ulcer.

3. Radiologic

Roentgenologists acknowledge that the X-ray is not infallible in the diagnosis of early gastric cancer, but together with the history and laboratory findings it usually completes the evidence in the type without previous history. When the tumor is situated at the pylorus, in the antral portions of the stomach, or along the curvatures, the radiologic indications of carcinomatous changes can be seen very early. Where the tumor follows upon an ulcer the differential diagnosis in the early stages is often very difficult. The X-ray is of especial service where the growth is on either of the curvatures or at the orifices of the stomach; here it will show infiltrations of the walls that cause them to become stiffened and lead to breaks in the peristalsis. These breaks, however, must be constant on all the plates or else they are of no significance.

George of Boston has called attention to the annular character of the filling defect in very early pyloric carcinoma.

Tumors in the body of the stomach, particularly in the posterior wall, may attain a large size without becoming evident under the X-ray, but a constant thinning of the bismuth shadow is an early indication of centrally located gastric carcinoma.

Postive X-ray findings place the case into the surgical category for at least exploratory incision. When negative X-ray findings in very early cases contradict strong clinical and laboratory evidence the patient should be kept under supervision and treatment and the radiographic examination repeated at frequent intervals until the case is cleared up.

The cases herewith presented illustrate and emphasize the writer's viewpoints. In these, the diagnosis, though necessarily formed on suspicion and not on proof, was vindicated by the histological reports of pathologists of recognized standing, and these reports are appended so as to leave no possible ground for challenging the results.

Case 1. C. L., age sixty-seven, seen November 27, 1917, stated that he had always been well until two weeks ago, when, without apparent cause, he suddenly vomited sour fluid three times in one day. Today, he again vomited with a very slight amount of blood. Since two weeks there has been almost constant epigastric heaviness, aggravated by food ingestion, and also increasing sitophobia. There has been no pain, but constant nausea, weakness, slight dizziness, pallor and loss in weight. Careful questioning elicited a long history of very rapid and excessive eating, of frequent sour belching and the avoidance of fried and sour foods and pastries. Two years ago, following a heavy dinner, there was a sudden, short

attack of unconsciousness with immediate recovery. Since then, on and off, there have been slight attacks of dizziness.

Physical examination. Showed a large framed man, moderately anemic and looking somewhat worn. The abdomen was soft, flabby and moderately pendulous; the liver border easily palpable, but of normal consistence; the abdomen was otherwise negative, excepting for slight point tenderness in the duodenal-pyloric regions. The stools were negative to occult blood. In the fasting state no stomach contents could be obtained; a test breakfast yielded 5i with free HCl 22, total acidity 34, no lactic acid, no occult blood; microscopically negative.

Röntgenological examination. Showed the stomach to be normal in position, size and shape, but revealed a constant irregular filling defect at the pylorus. There was rapid emptying of the opaque meal. The "cap" was filled and normal. The radiological diagnosis was "chronic ulcer at the pylorus with probable carcinomatous changes."

Operation. Performed by Dr. A. A. Berg on December 19 at the Mt. Sinai Hospital. A very large callous ulcer, too indurated to be regarded as benign, was found on the lesser curvature very near the pylorus. A total resection of the tumor mass and a posterior Murphy button gastro-enterostomy were carried out.

The following is the report of the examining pathologist, Dr. F. S. Mandelbaum:

"The ulcer of the stomach removed by Dr. Berg from Mr. C. L. is the seat of an extensive infiltrating carcinoma. Nests of carcinoma cells are present between the layers of muscle fibres down to the peritoneum. The mesenteric lymph nodes show an active metastatic process. In the nodes the carcinoma is distinctly adenomatous in type, while in the ulcer proper the type cannot be established absolutely."

The patient made a good recovery and has remained in excellent condition to date, three and one-half years after operation.

Case 2. Mrs. E. C. S., aged fifty-one, married, one child, referred by Dr. Van der Smissen March 2, 1912. For many years, immediately or a few hours after meals has had epigastric pressure relieved by belching of tasteless gas or sour fluid; also often nauseated after meals. Two of three protracted periods of marked epigastric burning relieved by medicine. Weight fluctuates since one year. Since about six weeks there had been continued nausea, but no vomiting, persistent epigastric pain only slightly relieved by food, and a constant sensation of fullness from the epigastrium to the throat, relieved by soda bicarbonate. Despite a ravenous appetite patient is losing weight. Two weeks ago and last night she brought up a rather large amount of bright red blood.

Physical examination. Slender, pale, highly emotional. Small cystic goiter. Mitral regurgitant murmur. The abdomen is soft, relaxed and contains a fair-sized, easily palpable, single uterine fibroid. One finger's breadth above and slightly to the right of the umbilicus is a circumscribed, hard, nodular mass about 2 inches long, freely movable and slightly tender.

A fasting stomach test yielded only 3ii of brownish yellow alkaline fluid, showing a few meat particles. One hour after test meal 3v of brownish yellow stomach contents, with few blood streaks; solids 3iii, mushy and poorly digested were aspirated. Free hydrochloric as well as lactic acids were absent. Total acidity 24; few gross and microscopic meat fragments. Stools negative for occult blood.

Diagnosis. Chronic ulcer with probable cancer. Operation was advised and performed a few days later, at the German Hospital, by Dr. George Semken. A freely movable and circumscribed tumor was found near the pylorus; few enlarged glands on the lesser curvature. The tumor, including pylorus, was resected, the stomach and duodenal wounds closed, and a posterior gastric-enterostomy done. The tumor was 2 inches long, was mostly made up of a shallow, round, indurated ulcer, only one part of which showed cancer.

The following is the report of the then pathologist of the German Hospital, Dr. Francis Carter Woods:

Gross appearance. Specimen consists of (a) small piece of tissue removed from the edge of a tumor of pylorus for diagnosis. It is firm and one section shows few small yellowish necrotic areas; (b) strip of gastric wall mucosa and muscularis removed from normal part of organ; (c) lymph nodes from pyloric region.

"Microscopic examination." (a) Shows adenocarcinoma, which infiltrates all layers of the wall. Composed of irregular gland structure and lined for the most part by a single layer, but in some places by multiple layers of columnar epithelium, which rests upon a distinct basement membrane. Stroma scanty and shows considerable infiltration (round celled). Mitotic figures not abundant. (b) Entirely normal gastric membrane. (c) Lymph node, the germinal centers of which are prominent. Peripheral sinuses show desquamated endothelial cells. No metastases found.

"Diagnosis. Adenocarcinoma of the stomach."

Patient is still alive nine years after operation and perfectly free from stomach symptoms.

Case 3. Mrs. F. J., aged fifty-four, seen in consultation with Dr. A. D. Mayer October 25, 1917. Always of a very emotional temperament; menopause nine years ago. For very many years has had mild symptoms of hyperacidity without definite pain, only heartburn. Since three years these have become more pronounced; particularly sour belching of gas or fluid with mucus. Diagnosed and treated then as a gastric neurosis by a gastro-enterologist. Periodic improvements and general well being until last spring, when, following a severe mental strain, the gastric symptoms returned, associated with sudden, weak spells with great depression and weeping. In particular, she had a continuous pain under the left breast which seemed to be connected with her stomach symptoms. Stomach analysis then showed total acidity of 15. A second examination a few weeks later showed 45, with some blood mixed with contents. String test negative. Gastric symptoms improved very much during the summer spent out of town, although patient found she had to keep to an anti-acid diet. Weight was practically always stationary. After her return to town in the fall, the gastric symptoms became more pronounced so that patient had been in bed most of the time. Dr. Mayer, who believed that the case was one of chronic ulcer, felt suspicious of a beginning malignancy and requested me to see the patient with him. She was well nourished but anemic and very weak. The abdomen was relaxed and negative to examination, excepting that there was an area of distinct tenderness, even to the slightest pressure in the left epigastrium, a little below the left costal arch. The feces were negative to occult blood. Only a fasting test was made and this showed no food retention. Our X-ray examination proved extremely interesting. It showed a rather large active

stomach, with a good sized constant pouch-like projection on the lesser curvature, which, in the oblique position, was demonstrated to be directly connected with the stomach. There was no six-hour residue. Our roentgenological diagnosis was that of a penetrating ulcer or an anomaly in development.

In view of the above data the diagnosis of chronic indurated, penetrating ulcer of the lesser curvature with probably adhesions and possibly carcinomatous changes was made. I advised against medical therapy, and urged operation. The malignant factor was suggested by the clinical features of the case. The patient was operated on November 7 by Dr. Willy Meyer at the German Hospital. A large indurated ulcer of the lesser curvature, penetrating into the left lobe of the liver and surrounded by a dense adherent inflammatory tumor, was found. One portion toward the pyloric end appeared suspicious of carcinoma upon gross examination. Microscopical examination of this part showed adenocarcinoma. Despite the extent of the tumor mass, a resection with gastro-enterostomy was successfully carried out.

Report by Dr. George L. Rohdenburg, Pathologist of the Lenox Hill Hospital:

"Mrs. F. J., November, 1917.

"Gross appearance. Specimen consists of a portion of stomach 10 x 5 cm. in diameter. Upon opening the organ there is found a crater-like ulcer with indurated margins 4 x 2 x 1 cm. in diameter. Its base is firm and yellow and in one portion there is a perforation-like slit, 2 x 2.5 cm. Section through wall of the ulcer is extremely resistant. At the border near the perforation is a yellowish mass, 0.5 cm. in diameter, directly beneath the base of ulcer and extending completely around the area of perforation.

"Microscopical examination. Stomach mucosa ulcerated over extensive area shows here and there remains of gastric tubules giving evidence of attempts at regeneration. In the yellow area situated beneath the mucosa there is an extensive development of carcinoma. The neoplastic cells are small, cuboidal and densely packed and supported by a hyaline, rather sparse stroma. In this area are many mitotic figures. Blood vessel or lymphatic channel emboli are demonstrable. The new growth has penetrated the organ wall to the serosa although it does not appear to have perforated this coat. Round cells and polymorphous infiltrations are extensive.

"Diagnosis. Carcinoma of the stomach arising in peptic ulcer."

Today, three and one-half years after operation, the patient is in good health and free from stomach symptoms.

CONCLUSIONS

1. The general pessimism as to the end results in timely-recognized and immediately-operated gastric carcinoma is not justified.

2. This applies particularly to cases in which the diagnosis has been predicated upon a thorough study of the clinical history and the faintest early indications, rather than upon the later appearance of the classical proofs of malignancy.

3. The signs described in the literature as characteristic of early carcinoma are so definite that a diagnosis made only after their

appearance is already tardy. More should be expected of the physician's diagnostic sense, so that the patient is operated early enough to have the best possible chance for cure.

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DISCUSSION

DR. FRANK SMITHIES, Chicago: The first question which comes in the office, when a patient has been proved to have a tumor is: "Doctor, will the operation make me well?" My pessimism is related to one group of cases, namely, that group in which there has been no history of a previous upset. I have seen none of those patients get well. When the patient has had long periods of gastric upset, previous to the evidently malignant stage, however, the prognosis is fairly good.

The post-operative follow-up of these cases has not been touched upon. I think it is very necessary. After the operation the best of hygienic and medicinal care should be instituted and with it Roentgen therapy from the first day the patient is able to be taken to the treatment room; particularly by the new method of high voltage treatments for a long seance. This treatment has been shown to be as efficacious as radium, probably much more so; but unfortunately there are few institutions in the country where this form of treatment can be given. I know of only two places. This is necessary to early institute these massive Roentgen treatments post-operatively, because of the histological and circulatory conditions at the site of the operation. At this time, there is an influx of blood and lymph for repair; there is consequent dilatation of all the capillaries. This very state of vascular engorgement of a repairing nature carries certain dangers. In consequence of it, there is simultaneously the greatest possibility for mechanical metastases. It is these metastases that kill the patient. Therefore, at this time it is most important that Roentgen therapy be pushed and pushed just as hard as possible, so that young mitosing cells in process of metastases may be destroyed before they are carried off, in the blood and lymph streams, to later lodge and grow in tissue outside their immediate origin.

DR. JOHN D. DUNHAM, Columbus, Ohio: Dr. Basch's paper is very timely because it indicates that internists are to be criticized along this line, first because they do not aid the general practitioner in earlier recognizing the importance of early operation in these cases; second, because they do not turn them over to the surgeon

soon enough and request early radical treatment in cases which can stand that treatment.

I have had 6 cases which have been free from recurrence after gastrectomy for three years. One case was a patient, forty-three years old, who had a sudden onset of gastric pain with vomiting of blood. Two months before he presented himself, a tumor was palpable in the epigastrium. It was clearly a case of cancer. The patient went on for three months before he submitted himself, and when the surgeon went into the abdomen it seemed to be an inoperable case. Fortunately we had a surgeon who had plenty of nerve, and he took out seven-eighths of the stomach, and the patient today is cancer-free. I do not think you can tell from the extent of the growth what the prognosis will be. This case was reported in the New York Medical Journal in 1912. Histological section made by Dr. Wood indicated a cancer.

DR. THOMAS R. BROWN, Baltimore: I have been interested in this subject because it is a duty that we owe to the general practitioner to preach the doctrine of early diagnosis in carcinoma. I have been interested in Dr. Dunham's report.

I have been interested in various points of view in regard to this question. The first point is in regard to the ulcer group, those which develop where ulcer was. It is not so much the finding of low acid, it is the finding of dropping acid plus the persistence of occult blood under rest and therapy which should be our sign-post as to the benign and malignant ulcers. In the second place, the group that Kussmaul describes, "which come like a thief in the night" without previous digestive history, these usually occupying the silent area of the stomach. I have been helped in this group of cases by the fact that if the symptoms do not yield in one month to rest and appropriate therapy one should give the patient the benefit of the doubt and operate. I think that in this group of cases it is absolutely justifiable because our only hope in this class of cases is to bring about operative treatment before we can make a diagnosis. In other words, we can only make a presumptive diagnosis. I was interested to find in a recent book by Sir Thomas Horder the same statement, that is, that if a patient in middle age with digestive symptoms with no apparent cause does not yield to rest and therapy in a month, he would advise an exploratory operation. And the same view is held by Robert Hutchison. If we wait for absolute diagnosis we will wait too long for the possibility of successful removal. Even in apparently inoperable cases it is justifiable to put the patient in the hands of a surgeon who will take risks to get results, because everyone of us has been impressed by the fact that in certain cases radical resection by a competent surgeon has produced results, not curative as a rule, but distinctly palliative in certain cases.

DR. LEWIS GREGORY COLE, New York: I should like to say one word in defense of the general practitioner. We look to him and perhaps criticize him for not detecting the cancer at an early stage? When I last looked up the cancers on which we had made a definite diagnosis, 49 per cent of those cases practically had gone to a stage where they were inoperable beyond any question of a doubt, either for palliation or cure, before they had given sufficient symptoms to justify them, apparently to justify them or to justify the doctor in having X-ray examinations. Now cancer comes as a thief in the night. I will quote this part from a paper I am going to

read "cancer comes like a thief in the night and gets a grip on the patient before the man is justified in having an operation on the patient." Now, how is the doctor going to know when to send the patient to a gastro-enterologist or to an X-ray man? It is just like cancer in the breast. How do women find cancer in the breast? Not by blood on it, not by pain; they are taking a bath and somebody else finds it for them. The growth of cancer unless it involves the sphincter of the pyloric end, gets to a size which is inoperable before it causes any symptoms. Now that is the hopeless part in the diagnosis of gastric cancer, and personally I see no way. I do see a way but I am not going to mention it at the present time for I do not think I have sufficient evidence. I will say—at the present time there is no way that one can detect these cancers at a stage when they can even hope for a radical cure except by a routine roentgenological examination once in six months or a year, the same as one should have a physical examination, and the same thing applies to cancer of the breast, women at the age of cancer of the breast should have their breasts palpated.

Now I say this in defence of the general practitioner as not having let the case get by him as inoperable, and that careful clinical history of a majority of these people, they will tell you that up to three or four weeks before they were just as well as they had ever been. Some of them will tell you that they had gastric symptoms for a long period—eight or ten years from the history, but that was not cancer; and I just say this in defence of the general practitioner on whom the onus of not making the diagnosis sufficiently early should not fall.

DR. MAX EINHORN, New York: I personally agree with Dr. Cole, and we should never put the blame on anybody in any case of cancer or any other disease; and I am always against that tendency of some other physician to say, "well, that one is to blame." But the truth of the matter is that there is quite a variety of cases. In some cases it is easy to make the diagnosis, and in others it is not, and in some cases we cannot make the diagnosis, even the surgeon operating with the cancer in his hand cannot make the diagnosis. I have seen such cases and the surgeon opening the abdomen say, "here we have a cancer," and it proved to be a benign case; and the reverse is true. Where you have to deal with such matters, where you have it in your hands and say that this is cancer when it is not, you will see that we are not able to make the diagnosis in every case and we should not blame anybody for not making a diagnosis.

Another point—the length of the disease is different. In some cases the symptoms will develop and when they are discovered it is too late to operate. Those are cases where there is so little to attract the patient's attention. There are other cases which are alarming from the start—the type and the position of the cancer and how it behaves.

Now in regard to X-rays, Dr. Cole thinks that if patients are X-rayed every six months, we will be able to discover these cases. That may be true in some cases, but I will mention a case I had in the hospital. A young lady of twenty-three came in with a tumor of her abdomen, and it was a tumor which was easily palpable, but it was different from the usual variety of cancer as the tumor could be moved from under the ribs on the right side way down to the symphysis, and by palpation it seemed to be like a cyst of the kidney. I examined her and found that I could feel the right kidney and I made the diagnosis of intestinal tumor, and radiograms were

taken. They were taken by a reliable man. She was X-rayed for two days. I said that the whole gastrointestinal tract should be X-rayed, especially the colon. The X-ray diagnosis was tumor outside of the gastrointestinal tract because there were no symptoms and the bismuth and barium came through, and the X-ray diagnosis was that it was not a tumor of the intestines or stomach. Now the surgeon in consultation said that it was the kidney because he took stock in the X-ray diagnosis. Before operating he said, "Where shall I make the cut? Because if it is a kidney, I shall have to cut in the rear, but if it is an abdominal tumor I shall have to cut in front." I told him it was intestinal and that he should cut in front. She was operated upon, and it was found to be a big tumor of the intestine, and the pathological diagnosis was sarcoma. It was as big as my fist and the lumen of the intestine was quite closed up, and still in such a case the X-ray diagnosis was not correct. So that, how can we say to patients who are healthy and well, "Go have your examination every six months in order not to get cancer."

Another point is the tendency to frighten people by telling them to look out. That will lead to a great deal of harm, more harm than if you let them go ahead even if some of them die; because if you frighten people, they will quickly get run down and get disease.

Now in regard to the other point, in regard to the possibility of resecting cancers and the patient remaining well—that is an event which happens very rarely but I have seen 2 patients on whom Dr. Meyer operated, the diagnosis being tumor, in whom a resection of the cancer was done, and one of them lived twelve years and died of heart disease while under my care.

DR. SAWYER, Cleveland, Ohio: I am also one who is not hopeful of the diagnosis of early cancer. I base my stand on the case of Miculic who had a cancer of the stomach. When he came to discover the cancer it was so far advanced that it could not be operated upon. If one of the greatest surgeons could not detect it on himself, what hope is there for the layman to get the diagnosis made on him? Yet in spite of this I think it is necessary to preach to the general practitioner and specialist the fact that cancer exists and that if anything is to be done, it must be done early. In spite of constant preaching I still think that we are not going to eradicate cancer by surgery.

DR. H. W. BETTMANN, Cincinnati, Ohio: I agree with Dr. Dunham and Dr. Brown that warning should be spoken about the duty we owe to the general practitioner. I think we have been led into great error by the interpretation of that phrase.

Now the indications for operation will be always by one of two groups; either by clinical intuition or insight or by definite signs which could lead us. Now the words "clinical insight or intuition" mean much or little; and this organization being dedicated to clinical insight, it is worthy of note that one of our members should have produced results in 3 cases where his clinical intuition led him to operate on early enough so that their lives could be prolonged, in 1 case nine years. The fact that he brings this before us is that clinical insight is so rarely found that these cases should be brought to our meeting. This means that in the last year our clinical insight has failed to save patients. Now here is a group of trained specialists whose clinical insight has resulted in saving a small group of patients. Ought we to go to

the general public and say that when your clinical insight on the diagnosis of a case is not progressing as you think it should, the case is one for operation? I think that is an erroneous stand to take. If our clinical insight saves only a handful, if you are going to the general practitioner to ask him to save a few, you are simply going to open the doors to a large number of surgical explorations and you are going to save of this number only an insignificant number.

Personally I think the advance is going to be along objective and not subjective ways. The duty of this organization is so to collect our material and so control the situation so that we can make our studies from objective signs which will enable us to have better results.

DR. JAMES C. JOHNSON, Atlanta, Ga.: I came in too late to hear the paper, but I want to say a word in the discussion and particularly with reference to early diagnosis. I am not as ready as some to excuse gastro-enterologists or surgeons or general practitioners who fail in the early diagnosis of cancer.

Some of you may remember, in a paper a few years ago I stressed the importance of all recognizing the primary nature of gastrointestinal diseases, and I believe that the main responsibility of the medical profession in failure to recognize cancer in its early stages, is from faulty education in colleges and of the public by the profession. The responsibility also rests upon many of the leaders of the profession, who speak the last word on this subject, for their failure to recognize the importance of the test meal and use of the microscope and other methods of examination.

Not until we educate the public, general practitioner and the surgeon, and place the burden where it lies on current newspapers and magazines, as well as the profession, and not until we recognize the importance of employing all means of diagnosis, will we make much headway in recognizing early cancer. As Dr. Smithies has said, there is but one sure way to make an early diagnosis of cancer, and that is by microscope; and the proper use of the microscope means repeated examinations of the gastric contents. There is no other way to get at it, and the profession will never get at it, until we adopt all these methods.

DR. WILLY MEYER, New York: It is laudable that the internists too have started the follow-up system in their patients operated upon. The literature amply proves that quite a number of patients suffering from gastric carcinoma can be saved. The case referred to by Dr. Basch was done by me on a lady who had advanced malignancy of the stomach. The proximal division was close to the costal arch. Still it was feasible to do the work by the Reichel-Polya-Balfour operation. I feel that if surgeons would more frequently resort to the osteoplastic resection of the costal arch in order to expose and make accessible the cardia, more patients with cancer of the stomach could be submitted to radical operation than are today. The additional operation is not grave, but naturally the surgeon is afraid of pushing his work too far, although I am free to admit that the surgeon should be bolder than bold in operating upon these patients who have 100 per cent mortality if nothing is done.

Of course, the great question also in gastric carcinoma is that which we call "virulence." Let me refer to cancer of the breast. There we often have to operate on younger patients, say between thirty and thirty-five years; we do the same radical operation as, for instance, in a patient of fifty-three for the same trouble.

But the younger woman rapidly develops metastases and dies, while the older one perhaps survives for twenty years and longer. It is that which we call virulence of the disease, having no better explanation, for, unfortunately, we still know little about the cause of carcinoma.

Lots of interesting points could be discussed referring to this subject, but I can touch on but a few. It was mentioned that patients who were not fat and who had a palpable tumor of the stomach should be operated upon and submitted to radical work—that certainly is correct. But stout patients should not be excepted. Lately a patient drifted into my office six years after operation; she had been stout; she had had no pyloric obstruction, but a large diffuse tumor on the anterior wall. I submitted the case to exploratory incision and found that the stomach was very large, so that I could divide within seemingly healthy tissue. I did a wide resection of the stomach and personally never expected to see this patient alive in the future. After six years she drifts into my office perfectly cured with red cheeks and in good health. It shows that operation on a stomach-wall tumor without involving the pylorus will sometimes give good results if a wide resection can be done.

After all, from a surgical point of view, very much depends on early diagnosis. If members of the Association could find reliable clinical or laboratory symptoms which would allow of early diagnosis of malignant disease of the stomach and justify the surgeon to do an early operation, it certainly would be a great achievement.

The same holds good for cancer of the esophagus. There, still more, much depends on early diagnosis, because after a little while the disease has gone too far and has involved important surrounding structures. I believe that the operative lull that we have had in this chapter, due to the treatment of cancer of the esophagus with radium, has passed and that an aggressive operative stage in the therapeutics of this disorder has again been reached today.

In closing, I will just touch the point brought out by Dr. Smithies. I thoroughly agree with him with regard to the necessity of X-ray and radium after-treatment. Particularly should we introduce into this work those powerful machines created abroad which seem to have a great depth effect.

DR. SIDNEY SIMON, New Orleans: An important element in the diagnosis is the character of the tumor. In the cases of scirrhus carcinomata of diffuse infiltration, I think the early diagnosis defies recognition. The softer type of tumors; the medullary type, an important point which was stressed by Dr. Brown, is the continual presence of occult blood reaction in the stools. I have had a case under observation last year which was quite on the border line between chronic ulcer and carcinoma. The patient was at the carcinoma age, but the clinical signs, the presence of increased acidity in the gastric contents, the lack of extreme pyloric block and the X-ray findings leaned more to the side of ulcer than of carcinoma. The patient felt that he did not want to undergo operative procedure unless the diagnosis of carcinoma was more certain. The patient was placed in bed, and though his clinical symptoms and the gastric distress subsided promptly with the dietetic treatment, still the persistence of the occult blood in the stools persisted and made me suspicious because it has been my experience in peptic ulcer with the treatment by diet and rest there is usually caused a cessation in the occult blood reaction in these cases. In spite of the subsidence of all clinical signs and

symptoms I felt that the time had come for operative procedure. On opening his abdomen we found a soft medullary type of adenocarcinoma in which we were too late to bring about recovery. It had invaded the posterior wall of the stomach so that total excision was deemed out of the question by the surgeon.

DR. R. WALTER MILLS, St. Louis: If I catch correctly the trend of sentiment, it is rather favorable to the surgeon, and I should regret to say anything that discourages that hopefulness. At the same time, if we will review the cases of carcinoma of the stomach and compare the number of cases which have been cured by surgery, they are but a handful as compared to the number in which the result has been tragedy. And yet I cannot but feel that we should do otherwise than strive in every way to meet the situation. The terrible thing is this—which is not often touched upon—that most cancers of the stomach never make a symptom until it is too late, or the symptoms are too vague to drive the previously healthy patient to a physician for having an examination and diagnosis. If a man is going to have cancer of the stomach, let him pray that it be prepyloric to result in insufficiency or let him be a thin man in which case he will have motor impairment. If a case occurs on the lesser curvature it will go to the inoperative stage before he will ever have a symptom of the thing. The X-ray helps us greatly, but it is most difficult to diagnose these early cancers of the stomach when they occur on the lesser curvature in test-tube-like form, when we have a concave lesser curvature.

I feel that the last word has not been said with regard to malignant degeneration of the early ulcer—about the crater being malignant. I have seen no case in which a crater became malignant. I have 4 in which it may have done so. My position is this—unless there be crippling of the stomach, I no longer operate on a gastric ulcer but treat it medically, unless it be a prepyloric lesion when it cannot be differentiated from malignancy. I have seen a number of ulcers penetrating into the pancreas with great craters, etc., that have undergone regression under a medical régime. The first case is seven years old, and the ulcer has recurred in attacks, and a break in gastric motility occurs at such time; the ulcer heals with rest and treatment. I say it with hesitancy, but we must be guarded in the diagnosis of prepyloric ulcer. It is difficult to differentiate prepyloric ulcer and syphilis from cancer of the stomach; and unquestionably the number of cures which have been reported as cures, are undoubtedly the resection of prepyloric luetic lesions, or rather a tumor which comes as a result of syphilis.

Just another thing—our most hopeful thing besides the X-ray is the test for occult blood but even in the early cases this fails because it means ulceration by the time it appears. The second is a little trick, and that is the palpation of these gastric tumors as observed by the X-ray, with the patient standing. It is a great trick. I can feel many of them standing, when you cannot get them with the patient recumbent.

DR. JULIUS FRIEDENWALD, Baltimore: I would like to warn against the plan that by placing a patient at rest and on diet we can accomplish much in clearing up the diagnosis of cancer. In my experience cancer patients often improve for a considerable period of time under rest and diet and frequently gain in weight for a time under such treatment; so that one is very apt to fall into error regarding this condition and I should therefore like to warn against this plan of caring for such patients until the diagnosis is definitely settled.

DR. LUDWIG KAST, New York: I believe that there is a very simple way of increasing the number of early diagnoses of gastric cancer. That simple way seems to me to lie in more frequent suspicion. We do not suspect cancer often enough, particularly the general practitioner does not suspect cancer often enough. It is again a case where mechanical devices are crowding out clinical studies and elaborations. If we wait for X-rays and fractional tests and for occult blood and for X-ray and other laboratory evidence, we shall be late in many instances; but if we train our minds—and it would be very regrettable if this Society should believe it to be almost impossible to make an early diagnosis because then we would only foster and strengthen an attitude on the part of the general practitioner which is responsible today for the large number of cases of carcinoma which remain unrecognized. We cannot make the diagnosis of cancer before we have the patient. We cannot make an early diagnosis if at the time the patient has his first symptoms and seeks medical advice it is too late. Now those two things are eliminated, I do not see how we can help that at the present time, but there remains a large number of patients who are diligently dallied with for months with hydrochloric acid and pepsin where it would have been a duty to suspect carcinoma and make the diagnostic effort by means of the X-ray which is one of the most important things. Then it would not come down to having everyone X-rayed every year to make the diagnosis, but when a patient shows symptoms of indigestion from any cause we ought to suspect carcinoma if he is in the carcinomatous age.

DR. SEYMOUR BASCH, New York (closing): I was much interested in the discussion which is always so important. It is impossible to answer all points that were brought out. Everyone who is conscientiously practicing medicine in private or in hospital practice knows how difficult it is to make a correct diagnosis and how often cases present themselves when it is too late. It has been my experience that people come to you far oftener when they have not a cancer than when they have one, especially middle aged individuals. And that is just the reason why we grow careless. We see so many patients who think they have a cancer and we venture a negative diagnosis and the case does turn out not to be a cancer. So, too, with cases with suspicious symptoms; we jump at a conclusion and get away with it. However, if we are as careful in our clinical work as the roentgenologist in his work is, and regard every patient with suspicion, I think even if we cannot oftener make a definite diagnosis of cancer, yet we will recognize the poor health and progressive downward symptoms of gastric disease and that is enough to justify our suspicions. Frequently we must content ourselves with a probable diagnosis, but we should not make it on subconscious intuition but only after broad minded medical study. Now you must not expect the layman to diagnose the case for you. The general practitioner often overlooks his case of carcinoma, but we, as specialists, should more profoundly study our cases. A few months ago I had a case referred to me where I felt a malignant tumor in the hypochondrium. The family doctor said, "I did not feel anything," and I said, "of course, you did not, you were too familiar with your patient to study him objectively enough."

If the case comes to operation the surgeon certainly should be one who works quickly. Nothing means so much here as the element of time. If a surgeon takes two hours to operate on a case that an expert would do in about half an hour, he surely is not the right man to do the operation, particularly if the case presents complications and he has to do more than he anticipated.

Dr. Smithies is right when he says that the prepyloric cases present a better chance for cure. I would not go as far as he does and say that those are the only ones that get well. I am surprised at the point he takes that they should be treated extensively with X-rays after operation for Ochsner in his chapter in Smithies' book on Gastric Cancer mentions cases with large secondary glands that were proved to be malignant metastases which eventually got well without X-ray or any further therapy. I do not want to disparage this treatment if there are men with established reputations who report curative results. I do believe my cases were definitely shown to have been carcinoma and I also believe that cases will get well after all with surgical treatment alone.

The final word I want to say is that we have to be progressive. We have to be progressive not only in using the things of established value, but in trying to bring into our armamentarium all promising methods suggested by others and try them out in a small or large way and stick to our own opinions. Very often we have to stand alone in our fight. Very often you cannot say any more than that a case belongs to the surgical category and ought not to be treated medically. We should, however, have good ground for our opinions in all cases and firmly maintain our ground.

BENIGN TUMORS OF THE STOMACH: REPORT OF TWENTY-SEVEN CASES

GEORGE B. EUSTERMAN AND ELMER G. SENTRY

Rochester, Minnesota

Benign new growths of the stomach, which because of their size or position may cause disturbed gastric function are rare enough to be regarded as clinical curiosities. In fact the great preponderance of gastric cancers over benign tumors of the stomach largely explains why the latter receive scant consideration in the differential diagnosis of doubtful cases. A pre-operative diagnosis of benign gastric neoplasm is exceedingly difficult in the majority of cases, and has rarely been made, at least until very recently. A great many of the cases reported in the literature have been found at necropsy and in the majority of those found at operation the true nature of the lesions had not been determined beforehand. In view of the importance of surgical conservatism in such a useful organ as the stomach the possibility that new growth is benign takes on a very practical aspect. Of further clinical and diagnostic importance is the fact that these tumors may cause complications such as pyloric obstruction, intussusception of the stomach into the duodenum, recurring severe gastro-enteric hemorrhage, strangulation, severe colic, malignant degeneration, and even perforation.

Two instructive reports on this subject have been presented before this association by the late Dr. Jesse Myer, and by Basch. For additional general reviews of the literature on the subject including excellent case reports and complete bibliographies, I would recommend the articles by Campbell, Merrill, Outland and Clendenen. Reports concerning specific portions of this material already have been published by two of my colleagues, Balfour, and Lemon, and by Nadeau and MacCarty in a pathologic abstract.

The material comprising 27 cases, all verified at operation is composed of 10 myomas, 5 fibromas, 4 angiomas, 2 dermoids, 1 gastric polyposis, 2 adenomas, and 3 polyps. Their histologic subdivisions will appear in the more detailed consideration of each group. These cases fall easily and logically into two clinical classifications, a primary

TABLE 1
Benign tumors of the stomach

CASE	SEX	AGE	LESION	(a) LOCATION; (b) SIZE	CLINICAL FEATURES
*19940	M.	66	Leiomyoma	(a) Two-thirds of pyloric ring (b) 5 by 7 cm.	Gastric disturbances, irregular type; indefinite colic pains; later ulcer type; palpable mass in epigastrium; hyperacidity; gastric retention
*44684	M.	45	Leiomyoma	(a) Antrum, near pylorus, cardia and esophagus, jejunal (b) 0.5 to 2 cm.	Recurring melena, occasional diarrhea; dysphagia. Anemia; diagnosed asymptomatic bleeding ulcer. Gastric analysis not made
*206857	M.	40	Leiomyoma	(a) Pyloric ring (b) Well marked muscle tumor	In many respects had a duodenal ulcer syndrome. Hyperacidity and hypersecretion
891	M.	62	Adenoleiomyoma	(a) Greater curvature just above pylorus (b) 1.5 cm. in diameter	Large ulcer on the lesser curvature with crater
77451	F.	60	Adenoleiomyoma	(a) Anterior wall of greater curvature 5 cm. from pylorus (b) 1 by 2.5 cm.	Cholecystectomy; appendectomy
209971	F.	28	Adenoleiomyoma	(a) Lower anterior wall (b) 1.5 by 2 cm.	Gastric neurosis
*40886	M.	48	Fibromyoma	(a) Posterior wall (b) 6 by 8 cm.	Three year ulcer type of complaint; melena. High normal gastric acidity; obstruction; tumor
*142665	F.	65	Fibromyoma	(a) 7.5 cm. above pylorus; posterior middle wall (b) 5 by 7 cm.	Chronic painful epigastric complaint; achylia. Movable, nodular tumor in left epigastrium; secondary anemia. Intussusception tumor with posterior gastric wall into duodenum

*236057	F.	35	Fibromyoma	(a) Anterior wall 3.5 cm. above pylorus and close to greater curvature (b) 2 by 1 cm.	Gastric disturbance of three months' duration. Severe attacks of pain. Tumor near pylorus "ball-valve." X-ray: filling defect in pylorus with large six-hour retention. Normal acidity
334803	F.	61	Fibromyoma	(a) Anterior wall (b) 2.5 in diameter	Pelvic inflammation; chronic cholelithiasis. Diabetes mellitus
*53373	F.	40	Fibroma	(a) Submucosa; pylorus (b) 3.5 by 2.5 cm.	Indefinite dyspepsia for two years, continuous for last five months. Discomfort one-half hour after meals; emesis gave relief; subacidity; mobile tumor
*86627	M.	36	Fibroma	(a) Pylorus (b) 8 by 5 cm.	History similar to that of duodenal ulcer of four years' duration. Hyperacidity; occult blood in feces
*208743	F.	16	Fibroma	(a) Pylorus (b) 3 by 2.5 by 2.5 cm.	Ulcer type of complaint and associated with duodenal ulcer; secondary anemia. Palpable mass in the right epigastrium. Prepyloric filling defect
241305	F.	51	Fibroma	(a) Not stated (b) Pedunculated; 7 by 2 mm.	Duodenal ulcer
*313898	M.	66	Fibroma	(a) Anterior wall (b) 1.5 cm.	Associated carcinoma of cecum; gastric history symptomless; X-ray showed lesion at outlet; moderate six-hour retention
*258233	M.	67	Hemangioma	(a) Anterior wall; body of stomach (b) 6 by 5 by 5 cm.	Complaint six months' duration; diarrhea; melena; two months' indefinite aching in left costal margin; two weeks' indefinite pain in right costal margin; sense of fullness with discomfort; appetite good, weight loss 25 pounds; free hydrochloric acid (roentgenogram shown in text)

* Primary cause for operation.

TABLE 1—*Continued*

CASE	SEX	AGE	LESION	(a) LOCATION; (b) SIZE	CLINICAL FEATURES
*324147	F.	25	Hemangioma	(a) Midway on greater curvature (b) 2.5 by 2.5 by 2 cm.	Atypical history; hematemesis, melena and diarrhea. Anemia; normal gastric chemism; ulcer crater in apex of tumor; X-ray showed lesions in posterior wall and greater curvature
*343572	M.	50	Hemangioma	(a) Anterior wall—bologna shape (b) 11 by 3 by 2.5 cm.	Dyspnea, weakness, severe anemia; no gross bleeding. Occasional emesis and sense of fullness after meals.
*356641	F.	22	Hemangioma	(a) Duodeno-pyloric (b) 7 by 5 cm.	Ulcer area 3 by 5 cm. on tip of tumor Dyspepsia since childhood, provoked by indiscretion; nausea and headache two to three hours after meals, sour emesis and relief; prevented by using soda before and after meals. Two acute attacks of epigastric pain six weeks prior to admission (roentgenogram shown in text)
*Pl.6206	M.	31	Dermoid	(a) Posterior wall (b) 7 by 6 by 5 cm.	Recurring hematemesis and melena; weakness; anemia (hemoglobin 40 per cent); no dyspepsia; free hydrochloric acid present
*136147	M.	8	Dermoid	(a) Posterior wall (b) 1000 grams	Upper abdominal tumor of gradual growth, of four years' duration; increased markedly in size in last six months; urinary frequency
*250518	M.	31	Polyposis	(a) Entire lower two-thirds of stomach	Indigestion for eight years; ulcer type of complaint continuous for past year; no nausea or vomiting; occasional diarrhea; no hemorrhage; loss of weight; achylia; mucus; characteristic X-ray findings
237007	F.	27	Adenoma (Brun-nerian)	(a) 1 cm. above pylorus (b) 2.5 by 1.5 cm.	Gall-bladder disease

2206	F.	30	Adenoma	(a) Lesser curvature 5 cm. above pylorus	Gastric neurosis; chronic appendicitis
80723	F.	29	Polyp (Adenoma)	(a) Near the pylorus (b) "Small"	Gastric resection for hypertrophy of the pylorus
220699	F.	20	Polyp (multiple) papillomas	(a) Throughout stomach and jejunum (b) 5 mm. to 3 cm.	Duodenal ulcer; second operation later for resection of jejunum
343402	F.	38	Polyp (Adenoma)	(a) Posterior wall 7 to 10 cm. above pylorus (b) 11 by 8 mm.	Gall-bladder disease; migraine; anemia; healed tuber- culosis at both apices

and a secondary; in the former group it was the presence of the tumor itself which caused the symptoms justifying surgical interference, while in the latter it was an associated or accidental finding during the course of an operation for other obviously major disease. A brief résumé of the entire series appears in table 1.

The 27 patients in the series were under observation in the Mayo Clinic between the years 1907 and 1921. During this period operation had been performed on 2146 patients with cancer of the stomach, on 20 with sarcoma, and on 2 with malignant polyps of the stomach, a total of 2168. The proportion, therefore, of malignant new growths to benign new growths is as 78 to 1, or 1.3 per cent of all gastric tumors were benign. But this proportion, in our own experience is only relative, for during the same period 2285 additional cases of malignant gastric neoplasms, the majority of them inoperable, passed through the Clinic.

Myomas. This group, of 10 cases, has been histologically subdivided into 3 leiomyomas, 3 adenoleiomyomas, and 4 fibromyomas. The 3 leiomyomas were classified clinically primary. Two of the patients (cases 19940 and 206857) were men aged sixty-six and forty-four, respectively. Both had a marked myomatous hypertrophy involving more or less of the entire pyloric ring and presenting palpable tumor, the first one 6 by 3 cm. in size. Both patients had distressing gastric disturbances over a long period in many respects simulating chronic ulcer. Hyperacidity and gross retention were present in the gastric contents of the former, and hyperacidity and hypersecretion in the latter. The third patient (case 44684) was a male, aged forty-five, with symptoms extending over a period of five years. The types of tumor were unusual in that they were mural and multiple in the jejunum and esophagus ranging in size from 0.5 to 2 cm. with one of medium size in the pyloric antrum. This case was characterized by recurring melena, occasional diarrhea, dysphagia, and anemia, but an entire absence of dyspepsia.

The 3 adenoleiomyomas ranged in size from 1 to 2 cm., 2 were juxta pyloric on the greater curvature, the third on the anterior wall in the first portion of the antrum. Two were found during the course of an operation for ulcer or gall-bladder disease.

The 4 fibromyomas are of considerable clinical importance since 3 of them were primary, the patient seeking reliefs from them. The first patient was a man aged forty-eight, with a movable tumor above and to the right of the navel. His dyspepsia was of three years' dura-

tion, strongly simulating ulcer. Gastric analysis revealed moderate hyperacidity and food retention. At operation a fibromyoma 7 cm. in diameter on the posterior wall, was removed. The second patient, a woman aged thirty-five, had had gastric complaint of three months' duration. The pain was usually severe. Gastric analysis and physical examination revealed normal conditions, but a filling defect of the pylorus, and a large barium residue was evident in the roentgenogram (fig. 1). At operation a small tumor 2 by 1 cm. was found on the anterior wall 4 cm. above the pylorus, close to the greater curvature. While the tumor was not pedunculated it could be manipulated as a ball-valve, which probably explains the course of the painful seizures. The case of the third patient, a woman aged sixty-five, is one of the most interesting in the series. She had had distressing dyspepsia for six years, progressive in character, with intermittent periods of food retention provoking emesis, and a palpable movable, slowly growing mass in the left epigastrium of four years' duration. She had lost more than 60 pounds in weight during the two years preceding her examination. For six weeks immediately prior to her admittance the patient had daily complained of irregular pains, of watery regurgitation and distress throughout the lower chest when swallowing and at times of regurgitation. Achylia and mucus were found on repeated gastric analysis, and a very unusual filling defect was revealed by the roentgenogram (fig. 2). She had secondary anemia. At operation (C. H. Mayo) a fibromyoma 5 cm. in diameter was found on the posterior middle wall of the stomach 7.5 cm. above the pylorus. The tumor, dragging with it the posterior wall of the stomach, had invaginated through the pylorus into the duodenum a total distance of 12.5 cm., forming an intussusception of a portion of the stomach into the duodenum. Wade and Collier have reported similar complications in benign new growths. In addition to these the museum contains three specimens of fair-sized myomas which have undergone sarcomatous degeneration.

Fibromas. The 5 tumors in this group occurred in patients ranging in age from sixteen to sixty-six. In 1 case, that of a small pedunculated fibroma, 7 by 2 cm., associated with a duodenal ulcer; the surgical records did not state the location, but the location in the remainder which were sessile, was definitely pyloric. According to the literature, this situation is the rule, although our specimens neither showed malignant changes nor represented fibrous growths at the site of old ulcers. Tumors varied in size from that of the smallest, already men-

tioned, to a diameter of 2.5 cm. Because of the position of the growth the roentgenogram revealed a filling defect in the pylorus and six-hour barium retentions (figs. 3 and 4, cases 208743 and 313898). In one patient (case 53373), a woman aged forty, symptoms of two years' standing, continuous and progressively more marked for the last five months, in conjunction with anacidity, retained food masses, palpable tumor and a pyloric filling defect, certainly justified the diagnosis of gastric cancer. In a second case a fibroma measuring 8 cm. by 5 cm. which involved the pyloric ring, presented a syndrome characteristic of duodenal ulcer of four years' standing with hyperacidity. A pylorotomy in this instance resulted in complete cure.

Angiomas. The four tumors of this group are histologically hemangiomas. They are exceedingly interesting because of their size and rarity. Lemon reported the first one of the series in 1920 and up to that time only 5 others had been reported in the literature. Two of our patients, both women, were in the second decade of life, 1 in the fifth, and 1 in the sixth decade. With 1 exception free hydrochloric acid was present in normal amount, and motility in all was unimpaired. With 1 exception the tumors were round, sessile, quite mobile at operation, of fair size, but not palpable on abdominal examination. They lay between the mucosa and serosa, were of soft consistency, and bluish black, or red; the 1 heretofore reported, situated in the fundus and anterior wall, on palpation suggested a mass of angle worms and the cut section resembled lung tissue (figs. 5 and 6). In the second case the rounded pedunculated growth 2.5 by 2 cm., was attached midway to the greater curvature and posterior wall (fig. 7). The ulcer crater in the apex of the tumor explained the bleeding and anemia. In the third instance an unusual bologna-shaped tumor measuring 11 by 3 by 2.5 cm. situated in the anterior wall was found. Dyspnea and weakness were the complaints presented, but on closer questioning an occasional sense of fullness after meals, and emesis were revealed. The patient, a man aged fifty, was very anemic (hemoglobin 44 per cent), gastric analysis showed an absence of free hydrochloric acid, a considerable number of fresh red blood cells in the lower power field and bits of tissue. These features, with the filling defect in the roentgenograms (figs. 8 and 9), strongly suggested cancer, and this was made the provisional clinical diagnosis. The feces contained besides the blood, pathogenic ameba and flagellates. The latter had probably provoked the

diarrhea. Erosion was found in the tip of the growth.¹ The last case, the only one of its kind to my knowledge, illustrates the diagnostic value of routine roentgen examination in all doubtful or obscure cases.

The patient, a woman aged twenty-two, was of a nervous temperament, and had had dyspepsia since childhood which was characterized by nausea and marked frontal headache, occasionally extending to the occiput, usually appearing two or three hours after a meal, and terminating in an hour or two by vomiting of sour gastric contents, followed by complete relief. These attacks were brief and intermittent, were often provoked by dietetic indiscretions, and in later years were prevented by small amounts of soda before and after meals. Up to within six weeks before her examination epigastric distress or pain had been absent but since that time she had experienced two violent attacks of pain in the epigastrium about four hours after a meal, preceded by the usual dyspeptic symptoms and terminating in emesis with relief. The patient attributed these seizures to excitement of moving in the first instance, and in the second to the hasty preparation for a trip. The physical examination was practically negative, except for moderate anemia which was attributed to a severe menorrhagia present since the onset of menstruation at fourteen. She was 12 pounds below normal weight. Gastric analysis revealed normal acid values with hypersecretion. The roentgenogram (figs. 10 and 11) revealed a large rounded, mobile mass in a dilated duodenum which was diagnosed benign tumor. At operation (E. S. Judd) a rounded sessile mass just without the pyloric ring about 7 by 5 cm., covered by a thin mucosa, was easily removed. It had the gross appearance and feel of edematous myoma, but on section and microscopic examination it proved to be a hemangioma. The patient is having an uneventful convalescence. The painful seizures can best be explained by a temporary complete occlusion of the pylorus by the tumor.

Dermoids. So far as I know only a few of these cases have been reported. Our first patient, a man aged thirty-one, was one of the earliest cases in the Clinic. For four years he had had recurring attacks of hematemesis and melena finally causing severe anemia and weakness. Free hydrochloric acid was present (hemoglobin 40 per cent). A tentative diagnosis of a symptomatic, bleeding peptic ulcer was made. Operation revealed a rounded tumor of the posterior wall of the stomach 7 by 6 by 5 cm. This was diagnosed dermoid by the pathologist. The second patient was a boy aged eight. About four years previously his parents had noticed a small lump in his abdomen, which seemed to be more prominent at times, especially when standing. The lump had enlarged gradually but during the six months prior to examination growth had been marked. Aside from some urinary frequency the

¹ A detailed description of the above 4 cases of hemangioma will appear in a paper by Doctor Judd.

patient had no symptoms. Examination showed a large movable non-sensitive mass filling the upper and central portion of the abdomen. A gastric analysis was not made. Roentgenograms did not reveal retention from the six-hour barium meal. The stomach was very high, occupying a transverse position. The displacement upward was due to a large palpable tumor which was extrinsic and did not deform the gastric lumen (fig. 12). At operation a gourd-shaped tumor, weighing 1000 grams was found attached to the posterior wall of the stomach and projecting into the lesser peritoneal cavity. The tumor was larger than the stomach itself. This was diagnosed dermoid cyst by the pathologist (fig. 13).

Gastric polyposis. This is probably the rarest form of benign tumor of the stomach. The only case seen in this Clinic has been described in detail by Balfour. He states that the tumor was then found for the first time out of approximately 69,000 abdominal operations, 8000 of which were for gastric lesions. Carman has seen only 2 cases in about 50,000 roentgen examinations of the stomach, 1 of which was the one described by Balfour; the other was the case of polyposis reported by Myer. As a result of Myer's own careful clinical observations over a long period in this case, and of similar observation made in the cases of Wegele and Chosrojeff, he states that gastric polyposis is more than probably present when such a combination of acute gastric hemorrhage, achylia gastrica, increased gastric motility and abnormal mucus production of an egg-white character is observed. Achylia gastrica, hypermotility and excess of mucus were present in our case, that of a male aged thirty-one, with distressing epigastric symptoms of eight years' duration. The roentgenograms in both cases are quite characteristic and show a diffuse mottled appearance of the pars pylorica and the lower pars media without six-hour retention or a corresponding palpable mass. This mottling is due to the displacement of the barium by the approximation of the polyps which, offering no resistance to the X-ray, produce numerous small, black shadows in the silhouette of the stomach (figs. 14, 15 and 16). Ruggles has recently reported 1 case with detailed roentgenologic findings. This tumor was described as a papillomatous rather than adenomatous structure, as originally described by Menetrier. Finney and Friedenwald reported 2 cases of gastric polyposis which had undergone malignant degeneration.

Adenomas. There were two of these tumors in the series, both were small and in women aged twenty-seven and thirty, respectively. The first tumor, 2.5 by 1 cm., was situated 1 cm. above the pylorus and

was a Brunnerian adenoma, first described by Hayem. It was mural, apparently symptomless and was excised during the course of an operation for gall-bladder disease. The second one, found during the course of an exploratory operation, was also symptomless and was a small, hard inflammatory adenoma, 5 cm. above the pylorus on the lesser curvature. Novak and Stretton have recently reported single pedunculated adenomas on the posterior wall of the stomach, near the pylorus, in adults, causing symptoms simulating those of gall-stone colic. The literature dealing with the various types of gastric adenomas has become fairly extensive.

Polyps. The term polyp in the clinical or descriptive sense signifies any small pedunculated tumor. The majority of polyps are undoubtedly mucous. We have restricted the use of the term to adenomatous or papillomatous growths in conformity with pathologic terminology. There were 3 of these in the series. All the patients were females, the tumors having been found during operation for other major conditions. Two of the polyps were adenomatous, both single, one small, near the pylorus, the other 11 by 8 mm. on the posterior wall, 7.5 to 10 cm. above the pylorus. In a third case, that of a woman aged thirty-eight, the polypi comprised multiple papillomas, scattered throughout the stomach and jejunum, and varied in size from 5 mm. to 3 cm. This patient had a chronic duodenal ulcer.

SUMMARY AND CONCLUSIONS

The 27 cases of benign tumors verified at operation, comprise seven different varieties in which are included myomas, with their histologic subdivisions, fibromas, hemangiomas, dermoids, gastric polyposis, adenomas, and polyps. They represent 1.3 per cent of all the gastric tumors operated on. Seventeen of the entire number were clinically classified primary growths because they were found to be the chief cause of the patient's complaint. Perhaps the most interesting group in this series, because of comparative rarity and size, is that of the hemangiomas. Twelve of the patients with this condition were males and 15 were females. The ages varied from a boy of eight with a 1000 gram dermoid on the posterior wall of the stomach, to a man of sixty-seven with a large hemangioma on the anterior wall and body of the stomach. The largest number, 7 in each, were found in the second and sixth decades of life. One-half of all the patients were more than forty. In 13 cases the tumors were in close proximity to the pylorus, in 5 they occupied the posterior wall, in 5 the anterior wall, and in 2 they were

generally distributed throughout the stomach. In 1 case in which the esophagus and jejunum were involved, and in 1, an early case, the records do not state the exact location. The size and shape of the tumor were variable because of the various types encountered. The majority were sessile rather than pedunculated. Gastric analysis and symptomatology afforded little aid in the diagnosis. Practically all the smaller tumors were symptomless. Seven patients had palpable tumors, 3 of which were fibromyomas, 3 were fibromas, 1 was a dermoid, and 1 a leiomyoma. The average loss of weight in the primary group was 25 pounds. Ten patients had recurring hemorrhage with anemia and weakness. This was chiefly due to ulceration or erosion of a portion of the tumor. Three of the 4 patients with angioma had severe bleeding and anemia. Seven patients had obstruction, this includes 1 patient with a fibromyoma of the posterior wall which had caused an intussusception of the posterior wall of the stomach into the duodenum. Severe, painful seizures simulating gall-stone colic were noted in several cases of juxta pyloric tumors which even though not pedunculated could be manipulated as ball-valve tumors. Myomatous tumors of the pylorus with or without pyloric obstruction simulate the duodenal ulcer syndrome. The roentgenologic appearance of the larger tumors is quite indistinguishable from that of gastric cancer.

Carman believes that a larger experience with this group will enable him to differentiate reontgenologically the two types more frequently than has been possible heretofore.

1. Benign tumors of the stomach are rare and constitute only 1.3 per cent of all gastric tumors that have come to operation. The actual proportion of benign new growths to malignant new growths or ulcerations is 1 to 200.

2. Myomas and fibromas constitute the largest group, gastric polyposis the most infrequent.

3. About 50 per cent of benign tumors are found in patients more than forty. There is no characteristic syndrome and gastric chemism ranges from achylia to hyperacidity with hypersecretion. The summation of evidence favors the diagnosis of gastric cancer.

4. The majority of the tumors are situated in the region of the pylorus, the greater curvature, anterior and posterior walls.

5. The smaller tumors are practically symptomless unless situated at the orifices, or unless multiple.

6. Common complications are recurring hemorrhage, which occurred in 37 per cent, and pyloric obstruction which occurred in 25 per cent.

Palpable mass, food retention, or six-hour barium retention is less frequent than in gastric cancer.

7. Often patients with benign gastric tumors are refused operation because the condition is regarded as malignant and inoperable. The true nature of the lesion is discovered only when the patients insist on operation.

8. The surgical end results are excellent.

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DISCUSSION

DR. WALTER A. BASTEDO, New York: Two years ago I brought to the museum exhibit of this association 5 specimens of polyposis of the stomach. Those were all collected in the preceding year and a half. They were all autopsy specimens except one that was obtained at operation. We have had 3 autopsy cases since. I think the statistics of those who attend autopsies will naturally be much larger than those of others. One of those specimens demonstrated the change from benign to malig-

nant. It showed 5 tumors, sessile or slightly pedunculated, 1 of which close to the pylorus was a complete adenocarcinoma, while 1 an inch away from the pylorus was slightly changed to carcinoma, the greater part of it being pure adenoma, and all the others were pure adenomata. As illustrating transition to carcinoma this case was instructive.

DR. J. C. HEMMETER, Baltimore: I wish to express my admiration of the paper, and I would like to know whether there is any numerical expression of the relative frequency of malignant to the per cent of the benign to the total number of cases. I missed the remark as to whether the entire stomach of the boy eight years old was excised at operation or whether that was an autopsy. I would like to inquire of all the speakers as to whether they have had any experience with tumors in the epigastrium which are phantom tumors.

DR. H. W. BETTMANN, Cincinnati: This is one of the subjects well worth bringing to the attention of the general practitioner so that he may know that these conditions do exist when his attention would be centered upon less important subjects when the occasion presents itself. It is surprising how sparse the literature is in reports of these cases; and more surprising is the inadequate knowledge or lack of knowledge of these conditions among surgeons and even among roentgenologists of wide experience. It shows again that we think mostly of those conditions in which we have had personal experience rather than of conditions which others bring to our attention. I will not take time to go into the clinical aspects because the time will not permit. Many of these cases go on without symptoms until something occurs such as a hemorrhage or a series of clinical symptoms which suggest malignancy or mechanical conditions, of course, such as obstruction or perforation or intussusception.

What I wish to speak more about today is the X-ray appearance, and I would like to report a further case which I saw this winter, making 4 in all. I brought along some lantern slides. I can talk in the dark from my notes. These cases usually bring up the question of malignancy, namely, recent gastric complaints with progressive downward course.

Patient referred by Dr. Baker of Newark, and gave a history of syphilis. We have to make a differentiation between the sessile tumors—those which are fixed upon the walls of the abdomen stomach and the pedunculated ones. This has to be made in the X-ray diagnosis because the sessile resemble carcinoma while the pedunculated involve the curvature and don't interfere with with peristalsis but cause mechanical obstruction when they get into the pylorus and cause intussusception and bleeding. This case (lantern slide) was verified at operation, but the patient collapsed and died. At autopsy in spite of the fact that this patient had some antiluetic treatment late examination showed this condition to be present (as shown on slide).

Next lantern slide: The bismuth could be seen trickling into the shadow defect. That was a point that Dr. Jesse Meyer brought out and that the defect impresses you as being finger prints. If you will recall the plate of Dr. Eusterman's, you will recall—this patient preselected a history suggestive of carcinoma, had lost weight and was anemic. Upon that picture (next plate) we ventured to make a diagnosis of malignancy, and the surgeon who operated upon this case said that he

never had heard of a benign tumor. The subject ought to be brought home to us and we ought not to condemn our patients to the scrap-heap as having inoperable carcinomata. I want to pass around some X-ray films that bring out that point. A man who had been sick for only two months, who had been condemned by three men, I believe also by Dr. Einhorn, as having an inoperable carcinoma and was told that nothing could be done, who presented identical X-ray films as I am passing around to you now, and who had a hemoglobin of 30 per cent, who, however, had not lost weight, who had not lost blood; he had no palpable tumor although he was a ptotic individual. He presented a large shadow defect, and a closer study of the X-ray pictures, as I will pass them around, will show you that one must not too lightly from X-ray plates make a diagnosis of carcinoma. On the greater curvature you see a large defect which is opposite the incisure and does not involve the greater curvature and does not cause any break.

One point more—in another position this shadow becomes smaller and smaller. In view of the clinical history and X-rays I ventured to say there was a 50 per cent chance of its being benign and also that it was a pedunculated tumor and on the posterior wall. This patient entered St. Luke's hospital and was operated upon and the diagnosis was sustained. He had a transfusion before operation.

This is a case that would fool us if we depended too much upon X-rays. This is a case which presented a tumor in the antrum and had a cancer history, but had no occult blood, but had an infiltration. She waited a month and a half before she was operated upon. At operation we found an extensive tumor in the antrum which had the landmarks of malignancy. She was operated upon three days ago and not reported upon yet.

DR. JULIUS FRIEDENWALD, Baltimore: I would like to present the plates of 3 cases of gastric polyposis which Dr. Finney and I reported at the meeting of the Association of Physicians in 1917.

DR. J. W. DRAPER, New York: I would like to report the occurrence of a hemangioma in a man forty years old. The most interesting point in the history lay first in the fact of its long duration and secondly in its enormous size. This patient was a physician who came under my observation about fifteen years ago. He had had hemorrhages ever since he was eighteen years old, recurring hemorrhages, almost to the point of exsanguination. Unfortunately no X-rays were taken. He was finally operated upon by Dr. Bull, Dr. Janeway and his pathologist being present. When the abdomen was opened the patient vomited an enormous amount of blood and Dr. Bull said to me, "There is no possibility of continuing the operation, the man has a cancer, it is inoperable and malignant and he will die, as you see." So he sewed him up. Contrary to expectations he made a very good recovery from this tremendous hemorrhage and about six months later said to me, "I believe my condition is benign; I wish you would operate." I said, "Very well," and I was just preparing to operate on him in three or four days but did not, and some four months later he had another hemorrhage, this being at least the two-hundredth hemorrhage that he had in the course of his life and he died. I immediately did an autopsy, took his stomach out and delivered it to our pathologist for examination. His report on it was about as follows: That it was a hemangioma of the stomach of the largest size that he could then find in the literature. It was the size of a human

placenta, measuring in transverse diameter as well as in thickness about that size. It lay on both the anterior and posterior aspects of the stomach and it extended to the serosa. I report this because I believe—or personally I have not seen in the literature the history of any such tumor of such enormous size and such extensive (long) clinical duration. It must have been there congenitally.

DR. G. B. EUSTERMAN, Rochester, Minnesota (closing): It was perfectly proper of Dr. Bastedo to call attention to some of the clinical and roentgenologic differential characteristics of sessile and pedunculated tumors. The main portion of my paper will embody some of my own observations in that respect. Doctor Carman felt that a more intensive study of all the collected and future material will enable him to discover roentgen features which may distinguish certain benign from malignant new growths. In this respect the study of a large series of gastro-jejunal ulcers and many cases of gastric syphilis with gross changes has made possible marked roentgenologic progress in this difficult field. I am obliged to support Dr. Einhorn in the contention that in the majority of our large tumors the impression we got from the X-ray evidence was the probable malignant nature of the tumor. In fact we frequently refused to accept such patients for surgery, and it was only on their insistence that they be explored that the true nature of the growth was determined.

In regard to Dr. Hemmeter's remark—he apparently did not get the point bearing on incidence that I made in the paper. These patients came under observation between 1907 and 1921, fourteen years. During that period I stated that 2141 patients were operated upon for various types of malignancy of the stomach so that the proportion of the benign tumors and the malignant tumors that were operated upon was 1 to 78. But that proportion is only relative because an additional number of malignant tumors so diagnosed, consisting of 2185 cases, came under observation during the same period. Now it is reasonable to presume that some of these were benign but the figures show the actual incidence is about 1 to 150.

The additional case reports of Drs. Bastedo, Friedenwald and Draper were very instructive.

SOME OBSERVATIONS ON HEMATEMESIS

CLEMENT R. JONES

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Knowledge of the conditions responsible for gastric and duodenal hemorrhage has not been greatly augmented by recent investigation, and the treatment has not been modified by any great advance for some years, so at the risk of bringing before you a subject on which the last word seems to have been pronounced, I invite your attention briefly to the escape of blood from the gastric and duodenal tissues into the lumen of the tract, in order to call your attention to what I have found to be a satisfactory combination of two remedies much used in controlling bleeding.

Changes in the spleen, the gall-bladder, the appendix and other foci of infection may be responsible for changes in the circulation of the gastric and duodenal tissues which lead to hemorrhage.

Referring to hematemesis due to hepatic cirrhosis,

Balfour cites the accumulating evidence that the spleen is responsible for certain types of hepatic cirrhosis and that early splenectomy will probably prevent further liver changes. That gall-bladder infection and appendicitis may be directly responsible for hematemesis has been shown by results of operations. It is more than very probable, however, that these or other foci cause the gastric bleeding by first setting up toxic changes in the liver.

The etiology of gastric and duodenal ulcer being yet unsettled there are some aspects of the bleeding resulting therefrom which remain also without explanation. One of the points of clinical significance which has interested us is the recurrence of bleeding or primary hematemesis after rectal feeding has been begun. Shortly after beginning the starvation period of some methods of treatment there will occur hematemesis which seems in some way to be the result of the treatment. An explanation of hematemesis occurring at this time might be found as a result of the irritation of the ulcerated surface by its apposition to the opposing gastric wall and to peristalsis activated by the nutrient enema. Erosions of the hemorrhagic type cannot always be distinguished from ulcer by clinical signs. The

string test will give evidence in both conditions, varicosity of either gastric or esophageal veins may be responsible for hematemesis or melena, these do not give an ulcer history, but the same can be said of some ulcers. We have hemorrhage in the ex-ulcer—*acio simplex* of Dieulafoy, acute or chronic gastric ulcer erosions, sarcoma, carcinoma, syphilis, cirrhosis of the liver, varicose veins, aneurysm of gastric artery, polypii, and ruptured cysts. It occurs as complication of diseases of the liver and portal system, spleen, pancreas, severe toxicemia and bacteremia of hemolytic character in purpura, scurvy, anemia and hemophelia in neuro-pathic conditions affecting the control of the circulation of the stomach as in gastric crisis of tabes, local injuries by trauma or of chemical origin, menstrual and climateric disturbances. Following operation where the circulation is affected with thrombi or otherwise, hematemesis may be arterial, venous or capillary.

It is evident that treatment aimed at the relief of a condition of such varied etiology must be based on very sound, broad and general principals directed at the control of the bleeding, in many instances when the cause is yet undetermined.

In reviewing the drugs which have been used with proved success in the treatment of hematemesis, a considerable number of remedies must be spoken of, acetic acid dilute, has been used in cases where there is transudation from erosion of the mucous membrane. Epinephrin in water has a transitory affect lasting from one-half to two hours. Cohnheim advises 2-drop doses of a 1:1000 solution of epinephrin in gelatin with lemon and sugar every three hours. It is advised by Stockton in 20- to 30-drop doses in $\frac{1}{2}$ ounce of water frequently repeated. Calcium lactate is said to be of value in increasing the coagulability of the blood; its usefulness has been questioned. Atropin as a vasodilator for the purpose of dilating the larger vessels thus draining the capillaries, is reported to be of value in capillary hemorrhage. Bismuth salts acting as local astringents are said to be effective in ulcer cases. Kaufman refers to its use by Kussmaul following lavage, using the crystalline subnitrate. Dr. Kaufman reports the successful employment of this treatment in his own work over a period of years. Gallic and tannic acid in 5- to 10-grain doses have been used for their well known local astringent effect. Lead acetate is prescribed in cases of hemorrhage from stomach, but is best known as a remedy in intestinal hemorrhage as in typhoid fever, being used in combination with opium. Terpin-

hydrate as recommended by Eustice Smith in Hemoptysis and Hematemesis. Poliakov, chief of the Clinic in Therapeutics of the Faculty of Medicine at Moscow recommended a solution of gelatin by mouth to be repeated two or three times a day and is so quoted in *La Union Pharmaceutique*, referring to its action as hemastatic in gastroragies epistaxis and other hemorrhagic conditions. Fluid extract of hydrastis acts in a similar manner to ergot, as does also hydrastin. Bastedo notes that after vomiting of blood thromboplastin, kephlin, coagulose or epinephrin should be introduced. Horse serum and transfusion are both valuable and transfusion especially when the red cells count falls below 2,000,000 and the hemoglobin below 40 per cent. The pressure cannot always be taken as an indicator as at the time of hemorrhage. The pressure is sometimes increased as a reaction or effort to maintain a balance, to accommodate the vessels to the reduced volume of blood.

This was brought forcibly to my attention recently in a patient with a systolic pressure of 220, who, having lost 3 pints to 2 quarts of blood had a systolic pressure of 230, an increase of 10 points, and twenty-four hours later, the systolic pressure was 180; a week later 160.

We may also use salt solution intravenously or by enteroclysis and hypodermoclysis.

Donaldson and Canac have a case of repeated hematemesis in a girl of nineteen years in which the red cells became reduced to 1,800,000 and the hemoglobin to 22 per cent. A direct vein-to-vein transfusion from her twin brother was followed in two hours by profuse menstrual discharge, more or less continuous for eight days. Five hours after the transfusion she was given 55 cc. of horse serum intravenously. This was followed in a few hours by her seventh and last hematemesis. After two subsequent transfusions she improved steadily and permanently. Recovery seemed due largely to the transfusion.

Morphin, 0.25 grain, as in other forms of internal bleeding seems to give both physical and mental quietude. Bastedo recommends strychnine to maintain gastric muscular tone.

The special treatment which I wish to call to your attention and emphasize is both systemic and local in its action and consists of the use of epinephrinized gelatin. The gelatin is prepared so that when cold it is of the consistency of molasses; to each tablespoonful dose is added, at the time of administration, 15 drops of 1:1000 solution of epinephrin, this to be thoroughly incorporated in the gelatin. The epinephrin being incorporated in the gelatin prevents its too rapid absorption thus giving a constant application of both

epinephrin and gelatin. The dose is repeated at two- or three-hour intervals, given by mouth and continued until occult blood is no longer found in the stool. Epinephrin combined with a gelatin, in the local and general action, meets the indications, by local action on the bleeding surface; being an astringent lubricant it is a food and in a general or systemic action has a stabilizing influence on nerve control of the organ. Epinephrin was recommended by Sajous in shock and proved of value in the world war.

These patients are, many of them, of the hypoadrenal type with low blood pressure, dilated stomachs, excess of hydrochloric acid, spastic colon and sometimes adrenal bronzing.

Dr. Kaufman reported a case of recurrent hemorrhage in an attorney showing remarkable feature of overwrought nerves preceded by prolonged, intense preparation of papers in presenting an important case in court. Such individuals may frequently be recognized as cases of adrenal exhaustion, and are favorably influenced by this treatment.

In my experience this combination has proved most satisfactory in the treatment of all forms of hematemesis and melena. It is to be supplemented when necessary by use of horse serum, transfusion and pressure by bandaging the extremities.

SUMMARY

First, allay as far as possible, the patient's fears. This is sometimes the most difficult part of the treatment.

All avoidable movements on the part of the patient to be prevented.

Absolute quiet in the room.

Attendants as few as can carry out the necessary treatment; no visitors.

Ice cap to epigastrium.

Morphine, hypodermatically.

Epinephrinized gelatin third hour as above, continued at increased intervals until occult blood disappears from the stool.

It has been my custom to call a surgeon in all cases, but the surgeons with whom I am associated have without exception advised against operation.

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DISCUSSION

Dr. JOHN A. LICHTY, Pittsburgh: Some five or six years ago I presented a paper to his Association upon the subject of hematemesis and called attention to the fact that some of these cases in whom starvation is suddenly established during the treatment, are more likely to have a prompt hemorrhage. While I have not used the gelatin in conjunction with adrenalin, I think that the point of Dr. Jones is a very good one. Yet we often have nausea and vomiting with these cases, and it seems, therefore, that it is not always practical to administer gelatin or any solution by the mouth. I wish to speak of a plan which we have adopted in the last few years and which can be carried on regardless of the nausea and vomiting, that is, blood transfusion. Formerly we allowed these patients to go on without surgical interference, hoping that the hemorrhage would finally stop. When the operation was finally decided upon the patient was already practically moribund. With the transfusion the hemorrhage frequently stops, but if it does not stop the patient's condition is kept at such a point that operation can be done more safely

at most any time. Transfusions can now be done very conveniently at the bedside; it does not take the nature of an operation and it does not in the least jeopardize the patient's life providing certain principles are recognized and the operator is familiar with the technique. Since this procedure I feel more comfortable with my persistent gastric hemorrhages than I have heretofore. Aside from the objection on account of the vomiting I think Dr. Jones' method a very good one and worthy of trial.

DR. SIDNEY SIMON, New Orleans: Three or four years ago I presented before this Association the records of several cases of hematemesis in which I thought the vascular factor played a rôle in its causation. These patients were of the cardiorenal type with high tension, and the hemorrhage of the stomach and upper intestines seemed dependent altogether on the arterial disease. Those cases I found from bedside observation, they having had several hemorrhages at intervening periods. Observing them, I thought after all the best plan of treatment was to leave them severely alone as far as medication was concerned, giving them the usual opiate hypodermatically and simple ice bag treatment. I found that any medication by mouth whether in the form of adrenalin or other drug that had been used, produced a tendency to vomit which I thought seemed to be harmful in causing a recurrence of the hemorrhage. I merely mention that.

Dr. Jones did not have a chance to go into the very various causes of hematemesis. I think we should specialize in the treatment, depending on the cause of the hematemesis. Some types, particularly the ulcer cases, will respond to the gelatin, and in various types by raising the blood pressure by persistent vomiting—such a method might prove harmful rather than beneficial.

A STUDY OF SIGNIFICANT CHEMICAL CHANGES IN THE BLOOD COINCIDENT WITH MALIGNANT TUMORS OF THE GASTROINTESTINAL TRACT

JOHN A. KILLIAN AND LUDWIG KAST

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The development of malignant tumors in the human organism is associated with such profound physical changes, that some significant alteration in the chemical composition of the blood might logically be expected, since the exchange of the anabolic and catabolic products of the tumor must take place by way of the blood. However, the results of such studies on record are surprisingly few, and in many instances contradictory. The most comprehensive analyses of the blood in malignancy have been reported by Theis and Stone (1) within the past year. These authors in a series of 189 cases, embracing a wide range of type of malignant neoplasm have found subnormal values for non-protein and urea nitrogen, particularly in the rapidly growing tumors of the breast and uterus, but an amino acid nitrogen slightly above normal. Numerous observers have noted similar findings for these components of the blood in normal pregnancy, suggesting an interesting analogy in the composition of the blood in malignancy and normal pregnancy. With the exception of two cases of melanoma, and malignancies with renal complications the uric acid was within normal limits or slightly below. Theis and Stone excluded all cases with renal involvement, but they do not state upon what evidence the diagnosis of renal involvement was made.

The concentration of the sugar in the blood in malignancies has received more consideration than probably any other factor. Trinkler (2) has found in all cancerous patients examined, a hyperglycemia which was more manifest in carcinomas of the internal organs than in carcinomas of the skin or mucous membranes. This increase in blood sugar, however, bears no relation to the development of cachexia. Cammidge (3) attributes the hyperglycemia associated with carcinoma to a disturbance of endocrine function. Of the

53 patients with malignant tumors examined by Benedict and Lewis (4), 36 per cent revealed a marked increase in blood sugar, from 0.12 to 0.16 per cent, and 49 per cent showed a tendency to a hyperglycemia. The blood was drawn in these cases three hours after the taking of food. The hyperglycemia was attributed by these authors to a constant demand of the growing tumor for carbohydrate. Rohdenburg, Bernhard and Krehbiel (5) found in miscellaneous cases of malignant tumors, normal blood sugar values, but after the ingestion of 100 grams of glucose they obtained hyperglycemias persisting for three to four hours. The blood sugar curves obtained bore no relation to the location of the tumor, or its nature (carcinoma or sarcoma), but closely simulated curves obtained after epinephrin injections, or in cases of hyperthyroidism. The suggestion is made by them that a probable explanation of the development of malignant neoplasms may be found in a disturbance of endocrine function. It is worthy of note, however, that glycosuria was not present in any case. A large number of the patients examined had tumors of the gastrointestinal tract. No allowance was made by these authors for the rate of absorption of the glucose, or for a possible renal involvement. Friedenwald and Grove (6), in like manner, obtained characteristic blood sugar curves after taking 100 grams of glucose. The control specimens show a mild hyperglycemia, which after the ingestion of the glucose rose to 0.24 per cent. The curve obtained in malignancies of the gastrointestinal tract differs from those observed in carcinomas of other regions, and therefore may be used as an aid in differential diagnosis. Of the 51 miscellaneous, malignant cases examined by De Niord and Schreiner (7), a hyperglycemia associated with an increased diastatic activity of the blood was frequently observed.

With the view of ascertaining the systemic effect of malignant neoplasms upon the human organism, the authors have studied the significant changes in the chemical composition of the blood in a series of 120 cases of malignancies of various types. The data accumulated comprise determinations of the non-protein and urea nitrogen, uric acid, creatinine, sugar, diastatic activity and carbon-dioxide combining power of the blood; the phenolsulphonephthalein excretion, the occurrence of proteinuria and casts, and the blood pressure. A few of the more salient clinical features of the cases have also been noted. The standard methods described by Myers (8) have been utilized in the analysis of the blood. In all instances

the specimens of blood have been obtained in the morning before breakfast. We have included in this series those cases in which the diagnosis of malignancy has been confirmed by operation, or by autopsy, with subsequent histological examination of the tissue. A few cases, however, were neither operated nor autopsied, but in these instances there can be no question of the correctness of the diagnosis. Further, we wish to emphasize the fact that the cases studied by us were not in a moribund state, on the contrary, they were patients who had presented themselves, many for the first time, at a general hospital, principally for diagnosis.

Of all the cases of malignancy, about 80 per cent show an increase of the uric acid concentration of the blood and about 60 per cent an increase of the urea nitrogen and creatinine, indicating more or less severe impairment of kidney function. The appearance and progress of this renal insufficiency follows the order of retention of the nitrogenous waste products described by Myers and his co-workers (8), for impairment of kidney function in general. The nitrogenous waste product first to be retained is the uric acid which is eliminated by the kidney with greatest difficulty, and as the involvement of the kidney function progresses there follows an accumulation in the blood of the urea nitrogen and finally of the creatinine. Although in this present communication data are presented only on a few illustrative cases of malignancies of the gastrointestinal tract, it may be said that this impairment of renal function was found to be invariably associated with general carcinomatosis, in 90 per cent of carcinomas of the bladder, prostate, uterus and rectum, and in about 50 per cent of the cases of gastric carcinoma. On the other hand, carcinomas of the breast and external epitheliomata produced no such changes. Of the small number of sarcomas coming under our observation, but one, a sarcoma of the kidney, showed a renal impairment. In all cases of non-malignant tumors, no disturbance of kidney function has been noted. This accumulation of the nitrogenous waste products in the blood was paralleled by a decrease in the phenolsulphonephthalein excretion. Although proteinuria was frequently encountered, casts were rarely seen.

It is worthy of note that impairment of kidney function bore no relation to the age of the patient or to the extent of the associated anemia. The observed changes in the blood cannot, then, be explained by a nephritis independent of the malignancy to be expected in patients of advanced age. In fact, the most pronounced reten-

tion of urea nitrogen and creatinine observed was in the case of a young woman of twenty-five years. A hypertension was noted in but 1 case, where there was other evidence of general arteriosclerosis. An examination of the ocular fundi revealed normal pictures in all cases with the single exception of the arteriosclerotic noted above.

The accumulation of these nitrogenous waste products cannot be attributed to increased metabolism produced by the growth of the tumors within the organism, inasmuch as the removal of the neoplasm does not decrease the concentration of these nitrogenous substances. In many instances anesthesia and surgical procedures provoked an acute exacerbation of the condition. The termination of many of the cases was typically uremic. It would appear, then, that the development of malignant neoplasms in the human organism entails an impairment of kidney function which is not accompanied by many of the clinical signs that we usually associate with nephritis.

Excepting the cases of carcinoma of the pancreas, a hyperglycemia and an increased diastatic activity of the blood indicating a lowered carbohydrate tolerance were encountered only in those cases manifesting a nitrogen retention. As this retention became more marked, the hyperglycemia and the increased diastatic activity kept pace with it. Apparently, then, the hyperglycemia noted by Benedict and Lewis, Trinkler and Cammidge, and the increased diastatic activity reported by De Niord and Schreiner must be attributed, not specifically to the malignant new growth but rather to the impairment of renal function. In like manner, the high blood sugar curves persisting after the ingestion of 100 grams of glucose by cancerous patients described by Rhodenburg, Bernhard and Krehbiel, and by Friedenwald and Grove, and considered by these authors to be characteristic of malignancy, find an explanation in this disturbance of renal excretion, raising the threshold for sugar excretion. Further evidence in support of this explanation is furnished by the absence of glycosuria in spite of a marked hyperglycemia (0.24 to 0.30 per cent).

Four cases of carcinoma of the pancreas have been studied by us. In 2 instances the diagnoses were confirmed by autopsy, and in 2 instances by operation. In all cases a hyperglycemia (0.17 to 0.23 per cent) and definitely increased diastatic activity (20 to 30) were found. In 1 case there was a retention of uric acid only, and in another an increased urea nitrogen of the blood, but the impairment of kidney function here was not sufficient to account for the hyper-

glycemia and increased diastatic activity of blood. This increased diastatic activity and hyperglycemia, with the glycosuria, we believe, are of some diagnostic value in malignancies involving the function of the pancreas.

SUMMARY

The development of malignant neoplasms in the human organism, particularly tumors of the internal organs, involves a disturbance of renal function resulting in the accumulation of the nitrogenous waste products in the blood. However, many of the other findings generally considered characteristic of nephritis are lacking. The examination of the urine alone, therefore, is not a reliable index of the operability of such cases. Moreover, studies of metabolism in cancerous patients must include determinations of the kidney function as a possible influencing factor. The increased diastatic activity of the blood and resulting hyperglycemia may be diagnostic aids in detecting malignancies of the pancreas.

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DISCUSSION

DR. FRANK SMITHIES, Chicago: This to me was a very interesting and suggestive article, but there are certain things that should be considered here with respect to the interpretation of the work—not with the work itself, for that has been most excellently performed.

The first point which is very striking is the consideration of the dehydration and fluid concentration in these individuals. I think these evidences are very noticeable in all established malignancies; such facts, purely physical and mechanical cannot but lead to high values on study of blood sera or lymph. The next point is the question of the peripheral circulatory rate, and the accumulation or stagnation of material in certain body sections. These things have been shown in disease very graphically by Hewlett during the last ten years in his plethysmographic studies. The third thing is the duration of material fed in the alimentary tract. In malignancies

nancy, this means a longer time duration for absorption and similar delay in elimination. There is a possibility of chemic retention of normally excreted substances in this factor. We have observed many times in collecting the bloods (particularly in the early morning before the inception of activity physically) this tendency of delayed absorption and a delayed concentration in blood chemical values. The fourth thing that is interesting to me is the general diminution in B. M. R. in these cases. This is seen in many types of ailment, not necessarily malignant; in nearly all these cases when they are followed through we find quite similar accumulations in the blood stream or in the lymph stream to those which have been detailed by the essayist; and lastly one must consider the evidences of this defective elimination in association with starvation. I do not mean gross or acute starvation, but from deficient food absorption over long periods—that is, impending. Findings quite similar to those detailed occur pure starvation alone (e.g., hysteria, cerebral injury, etc.) without malignant disease. They may go on to the point of actual acidosis.

But to me this has been a very suggestive paper, and I am going to endeavor to follow through work specifically directed along these lines. However, I think we should consider these factors critically, not from the standpoint of how well the work has been done, but with respect to unbiased interpretation of the results which have been presented.

DR. LUDWIG KAST, New York: This paper has only been a by-product of a very large amount of work that has been carried out in the last ten years in our laboratory and wards to establish a clinical and useful foundation for the use of blood chemistry. We have come to the point of considering blood chemical examinations as routine measures in all cases that offer diagnostic problems. There is an enormous amount of work accumulated which was carried out by Dr. Killian and Dr. Meyer; and they are to be congratulated. The results are capable of various interpretations, and I am glad that Dr. Smithies has mentioned that. Our paper is merely the ascertaining of the results as we have found them before. We have been well maintained in our blood work from the standpoint of diagnosis. We have found that if a patient on whom operation is contemplated shows a blood chemistry above a certain level, the mortality is very high, and we have come to the point of declining operations on the point of the picture of the blood chemistry. Whether the changes in the blood are due to alteration of chemical balance in the tissues and circulating blood or whether they are due to eliminative deficiency of the kidney is very hard to determine. As yet we do not wish to commit ourselves to one or the other, though our laboratory workers are inclined to say that it is due to an impaired renal eliminative power. We must think of the kidney as a dynamic filter which goes within varying limits, but when toxic substances anchor in the secreting cells of the kidney there seems to occur a mechanism of retention which presents itself in findings as shown today. We make no claim of diagnostic findings in these cases of carcinoma. We believe, however, that these studies bear the possibility of some diagnostic possibility later on. We do feel entitled to claim value of a diagnostic sign in cases for operation. It is interesting that the changes in carcinoma and the changes in pregnancy where embryonic cells enter into the chemistry of the blood are very similar. It is also interesting that carcinoma in organs arising from the endoderm show it, whereas carcinoma of the organs arising from the ectoderm do not show it.

DR. J. C. HEMMETER, Baltimore: I noticed at the end of the chart that Dr. Killian has reported that some of the cases were treated with radium. How many cases were treated with radium?

DR. KILLIAN: A very small percentage, and these specimens of blood were taken before the radium treatment.

DR. HEMMETER: I was going to report an interesting case of an inoperable tumor of the mediastinum on which Dr. Halstead refused to operate. The case was treated by Dr. Howard Kelly by the radium method, and we took the blood picture. The blood nitrogen and blood sugar were increased by the radium treatment and the man—he took 14 treatments—every time after the radium treatment suffered from a psychosis and I had to stay up with him all night. It seemed impossible for the eliminative organs to get rid of this nitrogen and the new aroused sugar in the blood from subjecting the neoplasm to the radium.

THE CHEMISTRY OF THE BLOOD AND OF THE BILE IN CHOLELITHIASIS

JOHN C. HEMMETER

Baltimore, Maryland

In tracing the sources of the chemical constituents which enter into the composition of concretions in the gall-bladder, it is important to bear in mind the normal constituents of bile and their physiologic derivation. Then, from this knowledge, we get a clearer understanding of the sources of the constituents of pathologic concretions. It can thus be clearly established that some of the substances that enter into the formation of gall stones are formed in the liver itself; others are derived from the blood; and still others cannot as yet be definitely traced either to the blood or to the liver. The bile salts, for instance, are produced by the liver cells and as their precursors we find the tissue proteins and the hemoglobin of the red blood cells, for there can be no doubt that the sulphur contained in the hemoglobin is eliminated in the taurochloric acid.

In connection with the bile salts, it must be borne in mind that after they are excreted into the intestine, they are not lost by the feces, but as Schiff has shown, there is a circulation of bile salts, which means that a certain proportion is re-absorbed. In the intestine, fat is split into glycerin and insoluble fatty acid; this latter is soluble in bile salts, and in this way is absorbed with the bile salts, which get to the liver by the portal vein, to be excreted over again (Schiff's circulation of bile salts). On the other hand, some of the bile salts are split in the intestines into glycine, taurine and cholalic acid, and some of these substances are absorbed as well. Some of the glycine may be converted in the liver into urea, some of the taurine into organic sulphates, which are found in the urine.

ORIGIN OF BILE PIGMENTS

The bile pigments, bilirubin and biliverdin, are formed from the hemoglobin which is derived from disintegrated red blood cells. The elements C—H—O and N of the hemoglobin enter into the formation of

bile pigments and the sulphur is eliminated in the sodium taurochlorate; the iron of the hemoglobin is deposited in the liver cells, to be used over again in the red bone marrow, to help to build up more hemoglobin, which is carried away in newly formed red blood cells.

In this connection I must very briefly refer to a histologic element in the liver, which is very rarely dwelt upon in connection with liver metabolism. I refer to the Kupffer stellate cells which occur in the endothelial lining of the blood capillaries of the liver.

FUNCTIONS OF THE HEPATIC KUPFFER CELLS

These cells have a marked phagocytic power (Kupffer-Maximow). The object of the phagocytosis is the inglobulation of primitive or decadent erythroblasts. These primitive blood cells are remnants of undeveloped cell forms. It has become quite certain that the Kupffer cells participate in hemolysis under physiologic conditions.

THE NET OR GRATING FIBERS SURROUNDING THE CAPILLARIES OF THE LIVER

These fibers were first described by Kupffer and they require a very delicate staining technique for their demonstration. They are very delicate fibrils that are spun around the blood capillaries in forms of an extremely fine and close meshed net. In the center, and also in the peripherie of the acini the fibers are in connection with the connective tissue of Glisson's capsule; on the other hand, they are in connection with the adventitious tissue of the central vein. Therefore, the entire parenchyma of the liver is permeated with these fibrils. They seem to represent an extra adventitia of the capillaries. It is assumed by Kupffer that the reticulum which in the embryonic liver represents the mother substance of the hematoblasts, represent the first foundation towards the grating fibrilli; in other words, these fibrils are derived from the mesenchyme just like the Kupffer stellate cells and the hemogonia (hematoblasts).

In this connection, it is important to bear in mind that in intra-uterine life the liver functions as a blood-forming organ. The Kupffer stellate cells are active in adult life in the destruction of red blood cells (H. Eppinger), even under physiologic conditions. What the grate fibrils accomplished is not known. They appear later in the life of the liver. A liver that is poor in these grating fibers is supposed to be near its embryonic stage.

CHOLESTEAROL (CHOLESTEARIN)

For methods of quantitative determination (see Physiologic Chemistry, especially MacLeod: Physiology and biochemistry in modern medicine, p. 698 and 697; also Methods of Bloor, *Jour. Biochemistry*, 1916, xxiv; Medicine of Windaus; also, H. Eppinger: "Die Hepato-Lienalen Erkrankungen," p. 146). These two most recent of works, one an American and the other a European, agree fairly well on the amount of lipoids, especially cholesterol in normal blood. It may be stated as 0.71 per cent in 1000 parts of blood; this amount is increased in certain diseases, especially diabetes and certain forms of cholelithiasis. The average amount of cholesterol in the daily amount of bile secreted when it amounts to 460 to 570 cc. in twenty-four hours is 0.1 gram. Such exact quantitative determinations cannot be made on bile drawn by duodenal intubation. The figures are derived from the discharge from gall-bladder fistulas after operation.

To be of value for the interpretation of the cholelithogenic process, cholestrin determination must be made on the blood of normal individuals, on the bile as drawn through the duodenal tube from normal individuals, and the identical determinations on blood and bile must be executed on patients afflicted with various types of cholelithiasis. This work has already been done by Medak and Pribram (*Berlin Clin. Wochenschr.*, 1915, nos. 27 and 28; see also Eppinger, *l. c.*, p. 74-75). These tables give not only the amounts of cholestrin found in the blood and bile of cholelithiasis, cholangitis and icterus, but they show also the amounts of bile pigments and bile acids in twenty-four hours' secretion.

It is also evident from these tables that there are enormous differences in the quantities of these substances that are excreted in the bile in various diseases, but this much is clear, that in all conditions affecting the liver and biliary apparatus, the total blood cholesterin is increased, whereas the normal is 0.71 per cent, in cholelithiasis, it is 1.648 per cent, and in cholangitis 1.019 per cent.

The intimate relation between deglobulation, by which term I mean to designate the red blood cell disintegration or hemolysis, and the blood cholesterol is shown by the subnormal total blood cholesterin in pernicious anemia. In a case (Eppinger, *l. c.*, p. 75) in which there were 1,500,000 erythrocytes and only 30 per cent hemoglobin Sahli, the cholesterin was 0.629 per cent; therefore, such blood disintegration would lead to increased pigments, which is indeed the case in the bile of these patients, but not to increase cholesterin excretion in the bile.

DISCUSSION

DR. MAX EINHORN, New York: I did not want to let the paper go by without a word. I enjoyed it very much. I want to make a remark about some particles which we find in the bile as it presents in the duodenum, especially in the darker biles where we find small, dark bodies about one-tenth of a red blood corpuscle. Usually they are dark, and I wondered what they were and I thought I could take them as some iron bodies, but I have also noticed some similar particles without that dark color, the same substance with the same shape only it looked as if the iron body had been taken out of it.

Now the whole subject is so interesting that I am quite sure that Dr. Hemmeter's studies will find further coöperation, and I want to express that I feel very grateful to him.

DR. JOHN C. HEMMETER, Baltimore (closing): A new pathologic histology of hepatitis and cholelithiasis points to the endothelial cells of the capillaries as sources of infection after they have been overworked in their phagocytic defensive function. The minute thrombi found in the capillaries of the liver in some types of hepatitis are composed chiefly of desquamated Kupffer cells.

NOTES ON HEMOCLASIC SHOCK AS A TEST OF LIVER FUNCTION

THOMAS R. BROWN

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Ever since Richet, apparently quite accidentally, discovered the reaction which he called anaphylaxis there has been increasing interest in this phenomenon and a rapidly growing group of diseases or abnormal conditions which have been regarded by many as due to this peculiar reaction. Very closely related to this, although differing in certain particulars, are the phenomena often roughly spoken of as shock due to the introduction into the circulation of various heterogeneous proteins—peptone, egg white, casein, blood serum, microbic proteins or the proteins of tissue destruction. The former represents the effect of a specific protein in a person or animal previously sensitized by the same protein, the latter lacks such specificity; desensitization, first suggested by Besredka, if properly carried out produces immunity for a considerable period of time in the case of the former, a very short or negligible time in the case of the latter, but the clinical features including the circulatory and hematopoietic phenomena are singularly similar in the two groups of cases. In both cases the symptoms, as a rule, clear up quickly if the result does not prove rapidly fatal. Both, if marked, are likely to be associated with dyspnea, arterial hypotension, collapse, various gastrointestinal symptoms, vascular phenomena, leucopenia with inversion of the leucocytic formulation, rarefaction of the hematoblasts, lessening of the coagulability of the blood as especially noted by Richet, Arthus, Biedl and Kraus and others; in anaphylactic shock the eosinophiles are likely to be increased, in nonspecific protein shock to be diminished or absent. Nevertheless each reaction really represents a similar picture—the picture of peptone, or protein or antigen shock. It can always be produced by the brusque introduction of heterogeneous protein into the circulation. Such clinical observations have been made for a long time, and it was Delezenne who first called attention to the fact that all the various phenomena were identical with those after the introduction of peptone. What is absolutely characteristic of

-anaphylaxis is the specificity of the reaction and the necessity of previous sensitization; of the protein shock its nonspecificity and the apparent absence of previous sensitization. But the two phenomena are of the same order and bring about the characteristic group of symptoms mentioned above.

It is hardly necessary to note that there may be cases of varying degrees of severity with a diminuendo of symptoms from the striking picture of severe anaphylactic or protein shock, sometimes ending fatally and always very terrifying to the patient, to symptoms so mild that only after the most careful study and analysis can they be regarded as in all probability referable to some form of protein shock. Unquestionably sensitization is brought about under ordinary conditions through various channels, as in the lungs by inspiration of bacteria and in the digestive tract by the ingestion of foodstuffs which may bring about the sensitiveness to specific proteins or a general sensitiveness to all proteins probably due to some disturbance in the defensive mechanism. Thus we may have a respiratory anaphylaxis possibly represented by some cases by asthma, and a purely alimentary-anaphylaxis as in many cases of urticaria.

Since 1913 Widal and his associates, notably Abrami and Brissaud, have devoted a great deal of time to the study of these phenomena, from these studies they believe that they are definitely able to diagnose this tendency, and by a specific test, "hemoclastic crisis." They also feel that they have shown that this hemoclastic crisis—that is, characteristic changes in the blood picture—usually precedes the other shock phenomena, and may be utilized in predicting subsequent symptoms; for instance it has been noted by them several hours before asthmatic paroxysms or urticarial outbreak of this origin, and they believe that this characteristic blood picture is an extremely faithful index of subsequent clinical anaphylactic or shock phenomena, while Pagniez, Pasteur Vallery-Radot and others have made similar claims in some cases of migraine, Danysz in certain cases of enteritis and certain of the neuroses and dermatoses and Widal himself sometimes in herpes. Widal has shown by a careful series of experiments that this shock phenomenon may in fact be brought about by the introduction of all kinds of heterogeneous proteins into the organism whether previously sensitized or not, by the respiratory or gastrointestinal tract, due to the growth and decomposition of bacteria or to the destruction of tissue in diseases as well as by the method of the original experiments, that is direct introduction into the circulation.

There has been an attempt, and in certain cases this is based on incontrovertible data, to explain certain other diseases and pathological phenomena on this basis. Among the diseases which have been ascribed to this cause may be mentioned paroxysmal hemoglobinuria, certain cases of asthma, hay fever, migraine, eczema, urticaria, and even epilepsy, while the malarial paroxysm is regarded by many as a phenomena of similar etiology. It is needless to call attention here to the view of many clinicians that in the case of true anaphylaxis the skin reaction after the injection of various proteins offers us a real proof of the sensitiveness or lack of sensitiveness on the part of the patient to the various proteins tested, although in our experience this has been extremely disappointing except in those diseases with definite skin manifestations, notably eczema, erythema and urticaria.

According to Widal and his associates as well as many other workers in this field, this shock is not a chemical but a physical reaction—"it is the index of a sudden perturbation in the state of equilibrium in the colloids of the body fluids" involving complement, sensibitric and antisensibitric, while according to Kopaczewski "anaphylactic shock and also all shocks produced by the introduction of foreign proteins are due to physical phenomena taking place between colloids and subject to the laws of colloid reaction." Thus in reality the picture is a colloidoclastic shock. That the nervous system plays a large rôle in its production is seen by the fact that if a general anaesthetic is administered the reaction is much less marked, and often in fact fails to appear altogether. The earliest localization of these shock phenomena, differing markedly in different individuals, here the lungs, here the skin, here the digestive apparatus, is probably determined by individual predisposition either congenital or acquired, and this seems to be the most rational explanation of the diversity of its manifestations, in one producing asthma, in one urticaria or eczema, in another severe migraine, while in still another some form of digestive disturbance. Certainly this conception of shock, either the specific anaphylactic shock or nonspecific protein shock as a simple rupture of physical equilibrium of colloid structures is far more helpful in explaining the rapidity and stormy nature of the symptoms, their rapid development and quick subsidence, than intoxication which must be regarded as a purely chemical process.

While Widal has been devoting much time since 1913 to the study of the more general phenomena of shock, it is only recently that he has attempted to utilize certain of its manifestations as a test of liver

function. According to the experiments of Widal, Abrami and Iancovesco the crystalline products of protein katalysis are not the only protein elements absorbed by the intestinal blood vessels. They believe and think that they have shown by experiment that at least during the early hours of digestion much more incompletely broken down proteins are absorbed which, under normal conditions, are prevented from reaching the general circulation through the medium of the liver—Widal calling this the proteopexic function of the liver. If this organ is functionally or organically extensively diseased this power is lost to a greater or less extent, the digestive proteins reach the general circulation and there produce definite symptoms of protein shock with the hémoclastic crisis as one of its early manifestations. He believes, therefore, that in this reaction he has a valuable test for liver function. While he has invariably obtained negative findings in normal cases, he has had many positive reactions in various diseases of the liver as, for instance, with chloroform or arsenobenzol poisoning; he believes that it explains many cases of digestive disturbances. From our studies we feel also that in certain of the vague and less well understood phenomena of various digestive disturbances as, for example, the somnolence after meals, so-called biliousness and certain digestive symptoms associated with headache, it is very possible that deficient liver function may be at the bottom of the process, and that the test that he has described may be the only evidence of a latent hepatitis. Widal found it in many cases of diabetes, and especially in toxic, bacterial or circulatory damage of the liver—in other words, in those processes which are diffuse. Widal, Galliot, Gerber and others have found it in a number of cases after the administration of arsphenamin, and believe it is more likely to be due to the drug than to lues itself; while Lenoir emphasizes the importance of latent liver insufficiency as the basic cause of many digestive conditions.

The technique of the test is very simple. While it would be interesting to test the coagulability of the blood, its cryoscopic index, its urea and non-protein nitrogen content and its azotemic ratio, and the inversion of the leucocytic formula, for practical purposes all that is really necessary is to study the total leucocyte count and the systolic blood pressure. The patient is given no food after 5 p.m. of the previous day. The next morning fasting the systolic pressure is determined and the leucocytes counted, three times at intervals of twenty minutes. He is then given 200 cc. of milk—Widal has

determined that it makes no difference what form of animal protein is administered as the reaction is not specific—and then at intervals of twenty minutes for one hour the leucocytes are counted and the blood pressure determined. In normal individuals there is no fall in blood pressure nor in total leucocyte count, sometimes, in fact, a slight rise in both. In those with disturbed liver functions the blood pressure drops 10, 15 or 20 mm. of mercury, while the leucocytes are diminished by one-quarter, one-third or one-half, or even more.

Every test that offers any hope of throwing light on the complex processes carried on in that most complex of organs, the liver, should, I feel, be carefully tried out by many men of many minds before it is accepted or rejected, and it is for that reason that I am presenting the present paper. We have tried out this test in between 25 and 30 cases—not a great number, but sufficient to furnish us with some data at least as to its possible value and application as well as its limitations. We have not tried it in cases of gross lesions of the liver—cirrhosis, carcinoma, or the chronic passive congestion of the cardiopathies; but have used it in those cases where possibly a deficient liver function—proteopexic, if you will—may play a part as one of the possible underlying causes. Thus, we have chosen a number of cases of headaches of the so-called bilious type as well as certain cases of migraine and other forms of periodic headache, cases with vague digestive symptoms as, for example, somnolence after meals, anorexia, lack of energy, chronic constipation often spoken of in the South as biliousness, in which the general and gastrointestinal findings were not sufficient to account for the symptoms, although, of course, in all such cases it is very difficult to gauge exactly the rôle played by unstable psyche, fatigue, worry, and other nervous phenomena, and it is, of course, quite possible that in many cases these alone could explain the entire picture. We have considered no reaction positive unless there was a drop of at least 2000 in the average leucocyte count. Most of our positive cases showed a drop of 3000 or more, while the systolic blood pressure drop—not so significant, I believe, as it is affected more by influences difficult to control, notably, of course, psychic and nervous influences—usually was from 10 to 20 mm. of mercury. Of our 25 or more cases 10 gave positive reactions, 5 gave what might be regarded as suggestive reactions, the remaining cases were negative. Perhaps the most disappointing result was that it was impossible to differentiate clinically those cases that gave positive from those that gave negative reactions. Thus in the headache

group certain cases with negative findings represented exactly the same clinical pictures in every detail as certain of the positive cases. Certain isolated findings, however, were very significant. In one case, for instance, of severe chronic emphysema with asthma when practically every protein had been tested as to the patient's sensitiveness towards it and absolutely no results had been obtained by dietotherapy based on these findings (in our experience a very frail reed to lean upon as a criterion of specific protein sensitiveness in this group of cases with the possible exception of the pollens and the hair and dandruff of animals) there was a constant leucopenia, never more than 4000 leucocytes, usually 3000 to 3500, and this dropped to between 2000 to 2500 after the test; a rather suggestive picture, I believe, of chronic non-specific protein sensitiveness increased by protein intake on the fasting stomach possibly due to lowered proteopexic liver function.

In all of our positive cases, even in our doubtful cases, and in fact in some of our negative cases, we tried the effect of small doses of peptone, giving either 0.5 gram of peptone or $\frac{1}{2}$ ounce of liquid peptonoids one hour before meals, and while the results were not brilliant, and as a rule, improvement was not marked, in a few cases the results were striking, but here again it was impossible clinically to differentiate these from the cases in which the results were almost nil.

Every one, of course, feels that one of the greatest impediments to our progress in a real appreciation of the digestive pathology and symptomatology is our almost complete inability to properly evaluate the functional disturbance of the liver in disease. Most tests suggested for this purpose have proven, in our experience, of little or no value—the levulose test, the urobilinogen and urobilin tests, etc., although in certain of the tests, notably the phenoltetrochlor-phthalein test, the direct obtaining of the bile by the Meltzer-Lyon method may prove to add largely to its value as also Rosenthal's method.

Perhaps the apparent unreliability of such tests is because we expect them to tell us too much; the liver is an organ of many and varied functions, it is hardly possible that any one test or method could give us data of value in regard to all these functions. This new hemoclastic test will also probably tell us only of the sufficiency or insufficiency of the liver as regards certain special functions relating possibly to the intermediary metabolism of the protein molecule, and it is not at all improbable that this function may bear little or no relationship to other hepatic functions of perhaps equal or even greater importance.

In fact, it must always remain a question whether another factor may not be involved to a greater or less extent in this reaction, that is an acquired sensitization on the part of the individual to animal proteins as a whole, or possibly to certain foods. I feel, therefore, that while the test is probably of value in telling us of certain possible variations from the normal of certain liver functions, and while it should be applied in selected cases as it is based on careful experimentation and clinical studies, its real value can only be gauged by its study by many clinicians over long periods of time before we can accept it as a reliable, test of liver function. But too much work has been done upon it already, treatment based upon such tests has been successful in too many cases, it comes with the approval of too good a group of clinicians, it is based upon too careful theoretical and clinical considerations not to make us feel that in a certain group of cases it may prove of real value and throw new light upon certain processes hitherto very obscure.

DISCUSSION

DR. FRANK SMITHIES, Chicago: I should not say anything, but I feel that if the paper is going to pass without discussion it might be taken as a lack of appreciation of the work of Dr. Brown. Dr. Ely, on my service, has been carrying on these tests, and we feel that some advance is being made. Just how great is that advance we are not ready to say. In our examination for the evidences of hemoclastic shock, we have considered it advisable that the patient go through the entire procedure at least once before we make our estimation for the record, in order that we may avoid any possible errors in the curve. For accuracy, and while the method is on trial it would seem advisable that the patient get accustomed to the procedure for three or four days before one makes diagnostic or any observations. Then when the patient is thus properly prepared, the "official" test may be made. This test is really a test of the "hold-back-ability" of the liver. It can be shown with sugars and with proteins. In other words, in disease, the liver is not able to prevent substances splitting up into the blood stream which have "leaked through" it by not being split up in the interior of the organ. This parenteral cleavage produces the normal response of a defensive leucocytosis and some slight increase in metabolic rate and body temperature. You will remember that in 1913 I published in the *Journal of the American Medical Association*, a paper dealing with the presence of a peptone-splitting enzyme in the circulating blood. We worked with the dipeptide glycyltryptophan. We showed that such peptide-splitting enzyme were normally present in the blood stream in health. In the hemoclastic shock test, this peptide-splitting enzyme acts on milk protein and splits it parenterally, when its complete transition through the digestive phase in the liver enables the protein to "leak through" the liver into the blood stream.

We have carried on the test in our service, but we are not yet ready to say how useful is the procedure, but on purely physiological chemic grounds it would seem that the test might prove of value in the estimation of liver function in certain groups of cases.

DR. THOMAS R. BROWN, Baltimore (closing): There is nothing more to say and I simply brought it up as one new method of trying to evaluate what is going on in the liver. It is a very simple test, but I do not believe we will know what its value is until it is tried by many men from many angles. What its value is I do not know as yet. It is sufficiently suggestive to warrant the attempt to use it.

CONGENITAL HEMOLYTIC JAUNDICE: REPORT OF AN INTERESTING CASE

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Cases of congenital hemolytic jaundice are of sufficient interest as well as rarity to warrant the description of an additional case.

Mrs. A. T. S., aged thirty-four years, entered the Church Home and Infirmary on September 1, 1920, with the complaint of jaundice and pain in the left upper abdomen. Her family history is of some interest. Her father was born in Germany, but moved to South Carolina in his youth, and died at seventy-one years of age with an obscure stomach disorder. He was jaundiced all his life, and was subjected to attacks of colic following which the jaundice would deepen. One paternal uncle died aged seventy-seven years, but the patient does not know that he ever had jaundice though two of his five children were affected with jaundice very definitely quite as she has been throughout their entire lives, and in consequence were frequently forced to discontinue work.

The patient has three brothers and one sister living; none of these were affected with jaundice, yet one brother who died of typhoid had had jaundice much like that observed in our patient. The maternal history is negative.

There are two children of the patient living, who are seven and four years old, respectively, and are both healthy. There is therefore a definite history of persistent jaundice in the patient's father and two first cousins; perhaps in her grandfather and brother. It is interesting to note that all of the members of her family affected with jaundice were males.

The patient was born and has lived all of her life in South Carolina. In addition to her occupation as housewife she has been quite active with farm work especially with cotton picking. She has always led an extremely regular life, taking much rest, and sleeping well, but frequently indulged in excessive eating. She drinks coffee freely, but is not addicted to the use of drugs or alcohol.

The patient had "dropsy" of the legs when five years of age, measles when thirteen, scarlet fever when fourteen; there is no history of malaria, rheumatism, tuberculosis or any other affection.

The patient has been jaundiced all of her life, but at times this discoloration deepens. Since her sixteenth year she has been affected with sharp acute pain, beginning under the right costal arch, and extending over the abdomen, and at this time she noted a deepening of the jaundice. Between these attacks she was usually comfortable, and had a good appetite, frequently overindulging in food. She has always been somewhat constipated, but her stools have never been clay colored, nor have they ever contained blood or mucus. With the attacks there was frequently

nausea and vomiting, the vomitus being bile tinged. The attacks of vomiting were accompanied with chilled sensations, fever and sick headaches. A diagnosis of cholelithiasis was made, and in December, 1911, gall stones were removed, and the gall-bladder drained. The attacks, however, soon recurred, and became so violent that in March, 1917, cholecystectomy was performed when numerous gall stones were obtained; at the same time an appendectomy was done. Since then the patient has no longer been affected with the attacks of pain originating in the gall-bladder region, but the acute attacks of nausea, vomiting, sick headaches, and chilly sensations have continued and with each attack there has been a rise of temperature with increase in the jaundice. A pain of minor importance under the left costal arch noted at the time of her last operation in 1917, has become greatly intensified with each attack, when the patient herself observed an enlargement and tenderness in this area. Even between the attacks there has been a constant aching in this region. There is in addition constant fullness and discomfort in the epigastrium and abdomen, which seems to bear little or no relation to the ingestion of food. Food does, however, at times produce some discomfort and indigestion.

The patient has herself been unaware of the enlargement of the spleen until informed of this condition recently. There is little else of importance in the history of the patient. Since October, 1919, she has had attacks of weakness and faintness, but without loss of consciousness. These sensations are aggravated by exertion, though they have made their appearance when the patient is at rest in bed. These attacks have been much less frequent during the past six months. The patient's power for sustained effort has been greatly decreased so that she is able to perform but little work. There is slight dyspnea on exertion.

The menstrual periods began between the seventeenth and eighteenth years, have never been profuse, and are fairly regular, and are not in any way related to the onset of the acute abdominal attacks. There have been no urinary disturbances, though the urine is frequently highly colored. The maximum weight of the patient has been 144 pounds two years ago, her average weight is 110 pounds, her present weight is 95 pounds.

Physical examination

The patient is a female, thirty-four years of age, poorly nourished and weighing 96 pounds. Her skin is smooth, and presents no eruptions or scars, but is markedly jaundiced. The icteric appearance is also revealed in the conjunctivae. The depth of the jaundice fluctuates slightly from day to day; being deeper following the attacks of pain on the left side. It is greater over the chest and abdomen, being nearly absent from the cheeks and hands. No glandular enlargements are present, the epitroclears, inguinal and axillary glands being barely palpable. The muscles are flabby and hypotonic and there is but little subcutaneous fat at hand. The eyes and ears are negative, the teeth normal, and the mucous membranes pale. The thyroid is palpable and slightly enlarged, no bruits can be elicited. The lungs and heart are normal.

The abdomen: The walls of the abdomen are thin and relaxed, the contour is flat. There are present two scars of former operations; a right rectus incision and a McBerny's; the liver is enlarged 2 cm. below the costal margin. The spleen

is elongated and easily palpable, extending in the mid-axillary line to 2 cm. above the crest of the ilium; the splenic notch is palpable. The spleen is of moderate consistency, tender on pressure, pulsations are not pronounced. The abdomen is markedly enteroptotic. The genito-urinary tract is negative and the reflexes are normal.

Laboratory findings

The urine: The daily output of urine varies from 1500 to 1850 cc. It has a specific gravity of 1020; is usually amber in color, though at times it presents a dark yellow appearance; it contains neither bile nor albumin (except a trace of albumin on one occasion); sugar is absent and the test for urobilin is positive. The microscopic examination is negative.

Phenol sulphone-phthalein test

	CUBIC CENTIMETER	PER CENT
Output for first hour.....	450	30
Output for second hour.....	400	11
	850	41

The blood: Wasserman reaction negative.

Red blood corpuscles, 3,200,000.

White corpuscles, 6,000.

Hemoglobin, 75 to 85 per cent.

Differential count

	FIRST EXAMINATION	SECOND EXAMINATION
Small mononuclears.....	30	28.5
Large mononuclears.....	12	7.5
Polynuclear neutrophiles.....	51	62.0
Eosinophiles.....	1	0.8

An examination of the blood smears indicates slight secondary anemia; no poikilocytosis and but slight anisocytosis; moderate polychromatophilia; no myelocytes; no nucleated red blood corpuscles.

Resistance of the erythrocytes to hypotonic salt solution:

Maximum, 0.48 first examination; minimum, 0.30.

Maximum, 0.45 second examination; minimum, 0.25.

The subcutaneous tuberculin test is negative.

Gastric secretion: Ewald test breakfast, 60 cc. of well digested clear secretion was obtained, total acidity 40 free HCl 32.

Rehfuss fractional analysis

HOURS	FREE HCl	TOTAL ACIDITY
$\frac{1}{4}$	20	32
$\frac{1}{2}$	26	34
$\frac{3}{4}$	42	58
1	36	48
$1\frac{1}{4}$	34	48
$1\frac{1}{2}$	228	40
$1\frac{3}{4}$	16	24
2	12	22
$2\frac{1}{4}$	6	20
$2\frac{1}{2}$	20	32
$2\frac{3}{4}$	20	34
3	64	80

Duodenal contents

The duodenal contents is yellow turbid and contains much mucus. On stimulation with magnesium sulphate, there is a free flow of very dark and cloudy bile, containing an almost pure culture of streptococci. A fractional analysis of the duodenal contents according to the Einhorn method is as follows.

	ALKA- LINITY	TRYPSIN	AMYLOPSIN	STEAP SIN
		mm.	mm.	mm.
Fasting stomach.....	20	4	2	15
$\frac{1}{2}$ hour after stimulation with bouillon....	18	1	5	10
$\frac{1}{2}$ hour after stimulation with bouillon....	20	6	2	10
$1\frac{1}{4}$ hours after stimulation with bouillon...	18	3	2	12
2 hours after stimulation with bouillon....	18	2	0	9

Stools. The stools are normal in appearance, brownish in color contain no blood, and but a slight trace of mucous. The examination for parasites and ova is negative. A few undigested meat fibers are observed and urobilin is present.

It was in 1885 that Murchison published a report of an interesting condition which he termed chronic acholuric jaundice, which was associated with anemia and splenomegaly, but did not present the usual manifestations of biliary intoxication. Subsequently LeGendre, Hayem, and Wilson reported similar observations, but it was not until 1900 that Minkowski clearly described the syndrome now recognized as congenital hemolytic jaundice occurring in certain individuals, members of the same family. Since then, numerous valuable contributions have appeared, regarding this affection. Among the most interesting cases published are those of Thayer and Morris.

These authors present an unusually valuable review of this entire subject together with a complete bibliography up to 1911.

Hemolytic jaundice may appear in one of three well established groups: the familial, congenital and acquired forms. According to Whipple and Harper this affection termed hemolytic jaundice is now established upon a definite scientific basis. It is possible that the rapid change from hemoglobin to bile pigment is brought about through the endothelium of the blood vessels, where great destruction of the erythrocytes takes place producing a rapid discharge of free hemoglobin into the blood. These investigators therefore conclude that hemoglobin can be rapidly altered into bile pigment in the blood without the action of the liver.

On the other hand, Naunym has called attention to the fact that not sufficient attention has been directed to the possible existence of obstruction in hemolytic jaundice. He is convinced that the liver plays a rôle in all cases and regards the jaundice as an infectious disease in which a cholangitis is an important factor. He feels that if more careful studies of the liver would be made, at least partial obstruction would be detected.

Recently Gerhart has also come to a similar conclusion and believes that careful repeated examinations will disclose symptoms of biliary obstruction.

The etiology of this disease has as yet, however, not been satisfactorily established. Hayem holds the view that syphilis is a prominent causative factor while Chauffard considers it due to congenital syphilis or to tuberculosis, to which there has been added some disturbance of the spleen.

It was Chauffard who first pointed out that there is present in this affection an increased fragility of the erythrocytes; in consequence of the increased susceptibility of the red cells to hemolytic agents, the anemia develops, the marked destruction of the red cells leading to an increase in the production of bile pigment; and, consequently, to icterus.

Others, as Banti, failing to observe hemolysins in the blood, assume that the destruction of the erythrocytes has its origin in the spleen and in consequence of the added work there is necessarily produced an enlargement of this organ. Widai, on the other hand, is strongly of the opinion that the destruction of the red cells occurs in the blood itself, and that the splenomegaly is due to the increased activity placed upon the spleen by the accumulation of the corpuscular debris.

In addition to the congenital form of hemolytic jaundice, there is an acquired form which appears in adult life with symptoms much like those present in the congenital type. This condition may arise without apparent cause or may appear after some acute disease or following an accident or may be associated with an acute infection.

The symptomology of congenital hemolytic jaundice is quite characteristic, the most prominent manifestations being chronic non-obstructive jaundice, splenomegaly and anemia, together with certain blood changes, diminished resistance of the red cells, and urobilinuria. Heredity is a most important factor in most instances.

The jaundice is chronic in character, and usually dates its appearance from birth or infancy; though it occasionally occurs later in life; it is not associated with bile in the urine or with clay-colored stools; it usually deepens at certain periods when exacerbation of the disease takes place. At times there may be a marked or entire disappearance of this symptom for a variable period of time. The enlargement of the spleen so characteristic of this affection is usually increased during the periods of exacerbation; at this time colicky pains usually manifest themselves in the splenic area and as the attack vanishes the spleen again diminishes in size; there is in addition a marked decrease in the osmotic resistance of the red cells to hemolizing agents; that is, increased fragility of these cells.

The method for determining the resistance is as follows: The red blood cells are separated from the plasma, washed and then placed in a series of test tubes in which are contained varying strengths of hypotonic salt solution varying from 0.7 per cent down to 0.36 per cent. In normal blood hemolysis begins at 0.44 per cent, and is complete at 0.36 per cent; in this affection however, it begins at some higher point, taking place at 0.6 or even 0.7 per cent. The blood changes usually present a moderate anemia, there is a deduction in the number of red cells with a decrease in the hemoglobin, the white cells usually presenting no variation from the normal; the red cells present a diminution in diameter, anisocytosis is present with polychromatophilia, rarely are nucleated red cells observed. Jolly bodies and basophilic granules are ordinarily noted. In addition attention has been called to the occurrence of a peculiar network of granules in the red cells when the blood is treated with a basis dye by means of post-vital staining. These are known as substantia-granulo-reticulo-filamentosa. These are abundantly present in hemolytic jaundice and are therefore of great diagnostic value.

The urine contains urobilin but bile is usually absent.

The stools are well colored, and contain bile and urobilin.

Post mortem findings: The autopsy findings as observed in a number of individuals by various writers are quite constant. There is usually present a marked siderosis of the spleen, liver and in less degree of the kidneys, and in no instance was there an indication of biliary obstruction.

In the treatment of this affection Banti reports in 1903 a complete cure by splenectomy. Similar results have been noted by Micheli, Frosi, UMBER, and Roth. In many instances as has been confirmed by Richards and Johnson, beneficial effects have followed the continuous administration of iron. In the congenital forms there is no serious interference with the patient's health, who may enjoy a fairly comfortable existence, many living to old age. The question of operation should only be considered when the symptoms become aggravated in the form of pain which may be due to biliary colic and which is accompanied by fever together with an increase in the jaundice. As a rule, however, aside from the jaundice these patients are usually free of the subjective symptoms ordinarily observed in jaundice; there being none of the signs of biliary intoxication present, ordinarily observed in this affection.

In conclusion, it is quite evident that the case presented by us represents a well defined instance of congenital hemolytic jaundice. In addition to the family and personal history the presence of chronic jaundice deepening at certain periods with exacerbations of the disease, and associated with anemia and splenomegaly, but without any manifestations of biliary intoxication points directly to this affection. There was present in addition a marked fragility of the erythrocytes. The urine contained urobilin, but was free of bile, while the stools were of normal color, and contained both urobilin and bile. Of some interest too are the findings of the contents of the stomach duodenum and of the bile. The gastric secretion presented normal values as to total acidity and free HCl on fractional examination up to three hours when a marked hyperacidity manifested itself (total acidity 80 free HCl 63). The biliary secretion removed with the duodenal tube was dark and cloudy and revealed a marked infection. Fractional analysis of the duodenal contents presented normal alkalinity curves with normal trypsin and unusually good steapsin values, but with quite poor amylopsin findings, which according to our experience is quite at variance with those observed in cases of obstructive jaundice, in which low values of all of the ferments are ordinarily noted.

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DISCUSSION

DR. WALTER A. BASTEDO, New York: One point that struck me in Dr. Friedenwald's case was that the fragility was not very marked. At St. Luke's Hospital we have tested a number of normal cases, and these showed 0.44 to 0.45 as the figure at which fragility or hemolysis began. In our hemolytic jaundice cases we have run as high a fragility as 0.65. Cases are reported with a fragility of 0.7.

One interesting case of congenital jaundice is a man in New York, a successful financier. He has no symptoms but has a yellow tint to the skin. If he exercises more than usual or is worried he becomes more yellow. Many years ago I found that he had no bile in the urine, though apparently jaundiced, and I was unable to explain this until some French articles appeared on hemolytic jaundice. We then found abundance of urobilin in the urine and the other features that distinguish the condition. Many of the congenital cases have no symptoms and are to all intents and purposes well. One lady had the spleen removed solely to get rid of the yellow color.

In one case in which there were bile as well as urobilin in the urine, a high fragility and a great many reticulated cells, we referred the patient to a surgeon for removal of the spleen; but as there was pain on the right side, as is so frequently the case, he refused to remove the spleen and took out the gall-bladder instead. The bile ceased to appear in the urine but the hemolytic jaundice went on. The patient had much nausea and vomiting and at another hospital had a gastro-enterostomy, followed three months later by entero-enterostomy for supposed post-operative vicious circle. Finally as the nausea and vomiting continued the patient came back to us,

and the original surgeon took out the spleen. She has been well since then. On account of the jaundice many of the cases have had the gall-bladder removed, some with real gall-bladder trouble and others without, but if the spleen is not removed the patients are not freed from the hemolytic jaundice.

DR. ALLEN JONES, Buffalo: It is very interesting to hear such a good account of so important a disease. I want to ask Dr. Friedenwald whether the duodenal contents also contained urobilin. One would rather say that the removal of the spleen being curative the condition points very strongly to some causative relation there. The formation of urobilin may arise from the transformation of hemoglobin by the endothelial blood vessel cells also.

These cases are important in ordinary routine because they require careful differentiation between the obstructive and hemolytic jaundice, and the question of complete jaundice and disassociated jaundice is brought up. This case was studied so clearly that it makes a valuable addition to our list.

DR. CHARLES G. STOCKTON, Buffalo: Dr. Friedenwald has entered so fully into the characteristics of hemolytic jaundice of the hereditary or familial type and of the acquired type that there is very little to be said except to compliment him upon the conciseness and fullness of his paper. I have had experience with both of these types and I want to call attention to only one fact that has interested me and which I have not been able to explain, that in certain cases of hemolytic jaundice we do not find the response to the hypertonic salt solution. The blood does not react to that as clearly and as definitely as you would expect from reports in the literature and the way it does react in other cases. Evidently there must be some other way of measuring the fragility of the cells besides that in these exceptional instances. I would like to know if the doctor has encountered cases of that sort. I speak of this merely as a reminiscence which I recognized and did not recognize, which I studied for a year or more and Dr. Allen Jones saw with me, and the case seemed to be different from any I had ever seen, and I sent the case to Dr. Osler, and he studied it and thought it was an unusual type of pernicious anemia. Five years afterwards he was in Paris in the Chauard in his experimental work on the blood cells, and Osler wrote of this case, giving me a diagnosis of this case, and I thought that might be of interest as showing Dr. Osler's mind and thoughtfulness.

DR. JULIUS FRIEDENWALD, Baltimore (closing): In regard to Dr. Stockton's question I want to say that there are some cases in the literature which are published which do not show the reaction to the hypertonic salt solution causing hemolysis.

In regard to Dr. Jones' question, the duodenal contents did contain urobilin.

PRIMARY CARCINOMA OF THE LIVER WITH REPORT OF A CASE

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It is generally recognized that primary carcinoma of the liver is uncommon, its incidence varying in different clinics from 0.13 to 1.3 per cent with an average of approximately 0.5 per cent in the collected necropsy reports. Despite the rarity many contributions to the clinical and pathological aspects of the condition have appeared in the past half century. The literature has been well reviewed by Hale White, Orth, Eggel, Wells, Goldzieher and Bokay, Rolleston, and Ewing, all of whom have added to the sum of our knowledge on the subject. As a result we have come to know that primary carcinoma of the liver seems to occur more frequently in men than in women, in contradistinction to primary carcinoma of the gall-bladder; that the most frequent age incidence is between forty and sixty years, although a definite type of malignant adenoma has been described in the young; that biliary carcinoma is seen later in life than liver cell carcinoma—the hepatoma of Rénon and of Sabourin; that the liver cell type is reputed as being from three to six times more frequent than the bile duct variety; that cirrhosis is considered to be the chief predisposing factor in about 85 per cent of hepatomas and in 50 per cent of biliary tumors and that the cirrhosis is usual portal and biliary in type and commonly alcoholic and syphilitic in origin. Since the diagnosis often offers as much difficulty to the clinician as the histogenetic interpretation to the morphologist and since the case at hand embraces many of the facts observed by others, the following data of the clinical and autopsy findings are presented.

The patient was a male of sixty-three who complained of being jaundiced and of noticing a dark-colored urine some five months previously. The onset had been gradual and was accompanied by a dull pain and slight soreness in the abdomen and the regions of the scapulae. The jaundice became deeper, the urine darker and the stools clay-colored, while weakness and loss of weight ensued and the abdomen became distended and the legs and scrotum began to swell. There had been no serious illnesses save typhoid fever. For years hemorrhoids had annoyed the in-

dividual. The patient was the father of two healthy children, his wife having had no miscarriages. Venereal infection was denied but he admitted to consuming whiskey regularly for a number of years.

On physical examination, there was evidence of weakness and loss of weight. The sclerae and skin were deeply jaundiced. The pupils were static. The abdomen was distended with fluid. The liver extended several inches below the right costal margin and the spleen could not be palpated. The scrotum and legs were edematous and the knee jerks were absent. A rectal examination revealed the presence of hemorrhoids and a normal prostate. The urine was 1020, acid and showed a faint trace of albumin, a large amount of bile and no sugar or casts. The hemoglobin was 68 per cent; the erythrocytes numbered 2,950,000 and the leucocytes 9500. The blood Wassermann was negative to lipoid antigen and positive to cholesterinized antigen, while the spinal fluid was positive to both, being under considerable tension and having 7 cells to the cubic millimeter. The pulse was 80, the temperature never rose above the normal and the blood pressure was 110-60 mm. Hg. The blood sugar was 0.10 and the coagulation time $5\frac{1}{2}$ minutes. The gastric analysis showed a normal secretion. About a month before death a rapid intensification of all symptoms appeared and a painless diarrhea developed. It became necessary to perform a paracentesis abdominalis, 3.5 liters of bile-stained fluid being removed. The patient became progressively worse and died an asthenic death. The clinical diagnosis was cirrhosis of the liver, probably syphilitic or alcoholic, or both. The painless jaundice, the extreme weakness and rapid progression of symptoms suggested the possibility of malignancy in the gall-bladder, bile ducts, pancreas or ampulla of Vater. Anti-luetic treatment had been instituted before death, with but little hope of beneficial results but with an idea of clarifying the diagnosis.

In addition to the tumor of the liver, a terminal broncho-pneumonia was found at the autopsy. There was marked icterus, ascites and edema of the lower extremities. The aorta was dilated and the arch showed evidence of syphilitic aortitis, while in the abdominal portion an extensive arteriosclerosis with atheroma and calcification occurred. The spleen and testes were fibrosed. (In the portal vein, at the hilus of the liver, was an ante-mortem thrombus.)

The liver revealed a marked biliary stasis and a diffuse biliary and portal cirrhosis.

The liver was enlarged, the rounded, inferior margin extending 4 cm. below the costal margin and 5 cm. below the xiphoid process. It weighed 2815 grams and measured 27 cm. in length and 17 cm. in width. The right lobe of the liver was prominent, being 15 cm. in thickness while the left lobe was shrunken and tongue-shaped. The organ was closely adherent to the diaphragm at the dome of the right lobe, and here the great omentum was reflected upwards and was attached to the hepatic surface. The surface of the liver was uneven and undulating, presenting a mottled yellow, brown, gray and green appearance. On the right anterior aspect, the surface was nodular over an area measuring 16 by 13 cm. The nodules were pink and yellow in color. They varied considerably in size and shape but all were flat, sessile and firm in consistency. The largest bulging occurred at the dome of the right lobe, being 2.5 cm. in diameter. On section, this area, which was softer than the surrounding tissue, was seen to consist of a soft, mushy, greenish purple tumor tissue. This structure was limited by a sharply defined structure

which looked like a thickened wall of an enormously dilated bile duct. The remaining surfaces of the liver were nodular and green in color—the result of an advanced imbibition of bile. It was apparent that the nodular character had resulted both from contraction of scar tissue and the bulging of tumor tissue. As a rule the nodules were large and rather indefinite in outline and did not simulate the hobnail type. The large character of the nodules gave to the surface a lobulated appearance. On section through the liver, it was found that the hepatic tissue in the right lobe had been largely supplanted by tumor tissue. The cut surface was uneven, the grayish-yellow tumor tissue standing out in marked contrast to the deep green liver tissue which remained. The neoplastic tissue occurred as irregular islands and finger-like projections which were extending peripherally and invading the adjacent liver substance in an arborescent fashion. As a rule, the neoplastic tissue lay in dilated channels and it was evident that the extension was occurring, for the most part, along the bile ducts. This effect was very clear in the central portion where the ducts were dilated, but in the more remote regions, the fibrotic, bile-stained liver tissue separated the gray, granular tumor tissue into islands. The unusual distribution of the tumor tissue at first suggested multiple foci but a closer inspection revealed the fact that the multiplicity was more apparent than real and that the peculiar arborescent nature of the growth had resulted from its direct extensions along biliary tracts. The larger collections of tumor showed central, yellow areas of necrosis. Where the tumor tissue was absent, the cut surface of the organ revealed a dark, green structure through which many heavy, radiating fibrous trabeculae coursed. At the hilus the portal vein was found to be dilated and filled with an organized, laminated blood clot. The inferior vena cava was clear. The gall-bladder showed a few fibrous adhesions at its tip. There was no evidence of tumor tissue along the extra hepatic biliary tract, or in any other viscus in the thorax or abdomen.

Microscopical examination of the liver showed a tumor growing in variously sized and shaped masses, apparently at the expense of the adjacent liver cells which were compressed, degenerated and contained a large amount of bile pigment. The tumor cell masses were separated by wide bands of stroma in which a moderate lymphocytic infiltration was noted. Necrosis of the tumor tissue was common and occurred more frequently and to a greater extent in the larger masses of closely packed tumor cells. Where, however, one could find smaller tumor masses, they appeared to be lying in channels lined by the low columnar epithelium of the bile ducts. In some instances, too, the character of a duct was preserved to a fair degree with the collections of tumor cells in the lumina, but in most of these the epithelium was interrupted by sprouting nodules of tumor cells or it became thickened by two or three layers of cells. Generally, there was in the tumor growth little resemblance to the normal bile duct. In many cases, though, the new cells were arranged a few layers deep on a supporting membrane and clumps of tumor cells, often necrotic, were seen in the lumina, indicating that even here some attempt at duct formation and differentiation had occurred. There was an increase of fibrous connective tissue around the portal systems here, the arteries and veins being clear. Often little masses of tightly packed cells were seen in the bands of the stroma. These were found with and without lumen formation and resembled regenerating bile ducts. The tumor cells on the basement membrane were cuboidal in outline while those near the center of the lumina were polygonal, polyhedral, oval or irregularly

shaped. The nuclei were large, vesicular in character, with a clear nuclear membrane and little chromatin arranged at the periphery. Many nuclear figures were seen. No bile could be demonstrated in the tumor cells. Where the tumor tissue was absent a moderate increase of connective tissue was seen, occurring as fairly heavy bands which were usually separating more than one lobule. The fibrosis in places was particularly heavy around the portal systems. The liver cells were often compressed and granular though the cell outlines were retained. The cells of the central zone of the lobules contain an excess of bile pigment, while the cytoplasm of those at the periphery were vacuolated, presumably with fatty deposits. The central veins were not dilated, but a few branches of the portal vein were.

There are many parallelisms between this case and those reported by others. The presence of a primary tumor of the liver in a male, well past middle life, who clinically presented a syndrome indicating a cirrhosis were both alcoholism and syphilis could have participated as etiological factors in quite a common combination in primary hepatic carcinoma. Clinically the case illustrates very well the difficulties in diagnosis and emphasizes that with an exacerbation and rapid progression of such symptoms as hepatic tumor, jaundice, ascites and cachexia, primary cancer of the liver should always be suspected. In this regard, it corresponds to the third group mentioned by Ewing, the others being those cases where no symptoms are detected, where latent carcinoma is found in patient's succumbing to cirrhosis or other diseases or where the history indicates from the first that a malignant tumor is developing in the liver of a previously healthy subject. Again, the dictum of Hale White—that after the appearance of a malignant liver tumor, life is seldom maintained over four months—obtains here.

Both in the gross and microscopically, the neoplasm closely simulated some which have been described previously. The situation in the right lobe, the tendency to multiple foci and the absence of metastases in distant viscera are well known characteristics of this type of tumor. Eggel found that the hepatic cell type of carcinoma was from five to six times as frequent as the bile duct variety. In this case the arborescent distribution and the inclination of the tumor to grow along bile channels indicate a probable ductal origin. Again, just as the cells of a hepatoma would be expected to differentiate like liver cells so the cells of the bile duct tumor should reproduce, to a certain extent, at least, duct-like structures. In the case at hand the morphology, arrangement, distribution and relation of the cells to the bile ducts, as well as their ability to form duct-like structures certainly suggest an origin from the epithelium of the bile ducts.

The relation of primary cancer of the liver to cirrhosis and vice versa has always been a moot question. Some investigators have held that the cirrhosis results from the carcinoma, others that the cirrhosis is a predisposing cause, while still others believe that the two conditions may occur synchronously. As a matter of fact, the arguments for or against any of these circumstances, are largely of academic interest. As Ewing says, "the cirrhotic process must be regarded as both contributing to and coincident with the tumor growth. There seems little point in the effort to disconnect these interrelations. A secondary fibrosis may develop about old nodules of liver-cell tumor, while biliary carcinoma is desmoplastic from the first." One could readily assume from the clinical evidence in this case that the cirrhotic process antedated the carcinoma. However, with the biliary stasis and the knowledge that a tumor process can stimulate overgrowth of connective tissue other than its own stroma, it is often difficult to determine how much of the cirrhosis is cause and how much is effect.

REFERENCES

No attempt has been made to assemble the numerous references in the literature on the subject. An extensive bibliography appears in the comprehensive works of Rolleston and Ewing. In recent years fewer articles have appeared, most of them having to do with the disease in young individuals or with the therapy of the condition.

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DISCUSSION

DR. JOHN A. LICHTY, Pittsburgh: There is nothing further to add except that just before I left the hospital to come to this meeting there was a case autopsied in which there was a tentative diagnosis of primary carcinoma of the liver, and which corresponded with the description of this case. The gross pathological findings of the liver in this case were almost identical to the case which I have just reported. However, when the esophagus was laid open throughout there was a small pedicle found in the upper portion which was malignant. The case was then, of course, put down as secondary carcinoma of the liver.

I wish to say in addition that in a large country consultation practice I see more supposed cases of primary carcinoma of the liver than are ordinarily seen in a large hospital. Most of these supposed primary carcinomas are found to be secondary and not a few are not carcinoma at all, being simply the enlargement of the liver due to an unrecognized cardiac decompensation. All of this illustrates the necessity of being careful in making a diagnosis of primary carcinoma of the liver and upon insisting upon having a complete autopsy made before such a diagnosis is accepted..

THE ACTION OF VARIOUS SALTS AND OTHER SUBSTANCES ON THE LIVER AFTER THEIR INTRODUCTION INTO THE DUODENUM

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SECOND SERIES

In a paper recently published (1) it was shown, as first stated by Lyon, that magnesium sulphate when injected into the duodenum, usually provoked a color reaction in the bile. The reaction in most instances takes place gradually, reaches an acme of color intensity (becoming very dark), then step by step diminishes, returning to a light yellow. The dark bile did not appear to be real gall-bladder bile as Lyon assumed, for the following reasons:

1. If the color change of the bile was due to the action of the magnesium sulphate on the gall-bladder causing an emptying of its contents, the change of color would necessarily be an abrupt one, beginning and ending sharply. This, however, is not ordinarily the case.

2. Magnesium sulphate, which is believed by Meltzer to relax Oddi's sphincter and by Lyon to cause the emptying of the gall-bladder, would in this way have no direct effect on the character of the bile evacuated. Solutions of 25 or 10 per cent of magnesium sulphate would, if the emptying of the gall-bladder is accomplished furnish a bile of identical color and other qualities. This, however, is not the case. The stronger the magnesium sulphate solution, the darker the color and the higher the specific gravity of the bile, indicating that the magnesium sulphate has a direct influence on the bile itself.

3. A great many other salts (which have no relaxing action) like sodium sulphate, bicarbonate of soda, and other chemicals act in a similar manner as magnesium sulphate, effecting the color reaction named above. The latter must be due to the action of these ingredients on the liver and the bile production, and not to a mere evacuation of the gall-bladder contents.

4. After applying the magnesium sulphate test, an immediate repetition of the test frequently provokes a reiteration of the same

reaction with its entire series of color plays. If the dark bile would be gall-bladder bile, the reaction could not take place anew right after the gall-bladder had emptied its contents.

5. Patients whose gall-bladders had been removed frequently give similar reactions after magnesium sulphate instillation, clearly showing that the gall-bladder as such can have nothing to do with this phenomenon of color changes in the bile.

Although the mentioned arguments are quite clear, it appeared worth while to repeat some of the given experiments and to increase their number in order to substantiate this view. This the more so as the power of the magnesium sulphate of evacuating the gall-bladder contents is generally accepted among the profession.

The studies on the action of salts and other substances on the liver after their introduction into the duodenum have been repeated and amplified. Besides magnesium sulphate, sodium sulphate, sodium citrate and magnesium citrate, bicarbonate of soda, chloride of sodium, calomel, mercurochrome and a great many other substances have been added to the list of drugs used in the investigations.

The identical method was used as the one described in the former paper, instilling a 60-cc. solution of the desired salt or some other ingredient into the duodenum at blood temperature and then to syphon it back by gravity.

In the following cases the new investigations will be given in concise form, with a few graphic representations:

Case 1. J. G. B., a patient with duodenal ulcer and chronic cholecystitis, had a complete series of different salts and other chemical ingredients instilled into the duodenum, so that a comparative study can be easily made. All these tests are briefly sketched and graphs given.

Test 1. March 8, 1921. Twenty-five per cent magnesium sulphate:

1. Fasting, orange yellow, very turbid; 10 cc.; alk. = 15; s. g. = 1010.
2. After six minutes clear and watery; 4 cc.; alk. = 20; s. g. = 1040.
3. After fifteen minutes light yellow, clear; 5 cc.; alk. = 20.
4. After nineteen minutes shade darker, yellow, clear; 5 cc.; alk. = 20; s. g. = 1020.
5. After twenty-one minutes, shade darker, yellow, clear; 5 cc.; alk. = 25.
6. After twenty-five minutes dark brown yellow, clear; 10 cc.; alk. = 30; s. g. = 1.020.
7. After thirty-two minutes lighter brown yellow, clear; 10 cc.; alk. = 25; s. g. = 1010.
8. After thirty-eight minutes yellowish green, very turbid; 10 cc.; HCl = 15; Ac. = 30.
9. After forty-one minutes yellowish green, very turbid; 20 cc.; HCl = 10; Ac. = 20.

10. After forty-seven minutes yellowish green, very turbid; 10 cc.; HCl = 10; Ac. = 20.

11. After sixty minutes yellowish green, very turbid; 10 cc.; HCl = 10; Ac. = 20.

12. After sixty-two minutes clear, dark brown; 2 cc.; alk. = 20.

Test 2. March 20, 1921. Thirteen per cent magnesium sulphate:

1. Fasting, canary yellow, turbid; 4 cc.; alk. = 15.

2. After three minutes light yellow, greenish tinge, slightly turbid; 4 cc.; alk. = 20; s.g. = 1030.

3. After seven minutes dark yellow, brownish tinge, slightly turbid; 40 cc.; alk. = 25; s.g. = 1010.

4. After fifteen minutes brownish yellow, slightly turbid; 40 cc.; alk. = 30; s.g. = 1010.

5. After eighteen minutes golden yellow, clear; 30 cc.; alk. = 20; s.g. = 1005.

Test 3. March 17, 1921. Thirteen per cent magnesium citrate:

1. Fasting, turbid, canary yellow; 8 cc.; HCl = 10; Ac. = 20.

2. Fasting, slightly turbid, light yellow; 5 cc.; alk. = 10; s.g. = 1010.

3. After three minutes watery, clear; 10 cc.; alk. = 10; s.g. = 1010.

4. After ten minutes light yellow, greyish, turbid; 10 cc.; HCl = 5; Ac. = 10.

5. After fifteen minutes light canary yellow, turbid; 10 alk. = 20; s.g. = 1005.

6. After twenty minutes light yellow, slightly turbid; 40 cc.; alk. = 20.

7. After forty-five minutes dark yellow, turbid; 10 cc.; alk. = 20; s.g. 1005.

Test 4. March 9, 1921. Five per cent peptone:

1. Fasting, canary yellow, turbid; 5 cc.; alk. = 20; s.g. = 1010.

2. After four minutes greyish, turbid; 5 cc.; alk. = 10; s.g. = 1010.

3. After seven minutes light yellow, slightly turbid; alk. = 25; 3 cc.

4. After eleven minutes dark brown yellow, clear; 5 cc.; alk. = 25; s.g. = 1020.

5. After sixteen minutes light brown yellow, clear; 5 cc.; alk. = 20.

6. After twenty-three minutes light brown, clear; 5 cc.; alk. = 10.

7. After thirty minutes light yellow brown, clear; 5 cc.; alk. = 10; s.g. = 1010.

Test 5. March 12, 1921. Eight per cent sodium bicarbonate:

1. Fasting, canary yellow, turbid; 5 cc.; alk. = 15.

2. After four minutes watery, clear; 5 cc.; alk. = 25; s.g. = 1012.

3. After six minutes dark yellow, brown, clear; 10 cc.; alk. = 30; s.g. = 1020.

4. After nine minutes light yellow, brown, clear; 5 cc.; alk. = 20.

5. After twelve minutes dark yellow, turbid; 5 cc.; alk. = 15; s.g. = 1010.

Test 6. March 10, 1921. Twenty-five per cent glucose:

1. Fasting, canary yellow, slightly turbid; 5 cc.; s.g. = 1010; alk. 20.

2. After two minutes clear, watery; 5 cc.; s.g. = 1020.

3. After four minutes light yellow, clear; 10 cc.; alk. = 20; s.g. = 1040; sugar = 1 per cent.

4. After six minutes dark brown, yellow, clear; 10 cc.; alk. = 25; s.g. = 1030.

5. After ten minutes light brown, yellow, clear; 5 cc.; s.g. = 1030; alk. = 25.

6. After fifteen minutes darker brown, yellow, clear; 5 cc.; alk. = 30; s.g. = 1021.

7. After twenty minutes brownish yellow, greenish tinge, turbid; cc.; alk. = 20; s.g. = 1010.

8. After thirty minutes light yellow, clear; 40 cc.; alk. = 15.

9. After forty minutes light yellow, clear; 10 cc.; alk. = 15; s.g. = 1010.

Test 7. March 11, 1921. Pilocarpine 0.005 gm.:

1. Canary yellow, turbid; 5 cc.; s.g. = 1006; alk. = 10.
2. After ten minutes light yellow, clear; 10 cc.; alk. = 10; s.g. = 1004.
3. After fifteen minutes canary yellow, turbid; 4 cc.; alk. = 20; s.g. = 1004.
4. After twenty-five minutes light yellow, brownish, clear; 5 cc.; alk. = 30; s.g. = 1005.
5. After twenty-five minutes dark brown, yellow, clear; 10 cc.; alk. = 30; s.g. = 1005.

Test 8. March 14, 1921. Atropine sulphate 0.0005 gm. in 60 cc. of water:

1. Fasting, canary yellow, turbid, greenish tinge; 10 cc.; alk. = 20; s.g. = 1015.
2. After four minutes, clear, watery; 5 cc.; alk. = 20; s.g. = 1005.
3. After five minutes, canary yellow, turbid; 5 cc. alk. = 20.
4. After seven minutes light yellow, brown, clear; 4 cc.; alk. = 25.
5. After nine minutes dark yellow, brown, clear; 5 cc.; alk. = 35; s.g. = 1005.
6. After twenty-five minutes dark yellow, brown, clear; alk. = 20; 5 cc.
7. After thirty-eight minutes dark yellow, brownish tinge, clear; alk. = 20; 40 cc.; s.g. = 1002.

Test 9. March 28, 1921. 0.5 per cent mercurochrome in 60 cc. of water:

1. Fasting, pea soup yellow, turbid; alk. = 20; s.g. = 1006; 10 cc.
2. After three minutes very dark red, turbid; 5 cc.; alk. = 15; s.g. = 1005.
3. After seven minutes very dark red, yellow, turbid; 10 cc.; s.g. = 1002; alk. = 20.
4. After fifteen minutes lighter red yellow, slightly turbid; 10 cc.; alk. = 25; s.g. = 1002.
5. After twenty-five minutes light yellow, reddish, turbid; 10 cc.; alk. = 1005.
6. After thirty minutes dark yellow, reddish, clear; 10 cc. alk. = 25; s.g. 1005.
7. After thirty-five minutes light yellow, reddish tinge, turbid; 10 cc.; alk. = 30.
8. After fifty minutes light yellow, reddish tinge, turbid; 10 cc.; alk. = 15; s.g. = 1010; (color altered by red of mercurochrome).

Test 10. March 11, 1921. 0.5 per cent saline; 60 cc.

1. Fasting, canary yellow, turbid; 5 cc.; alk. = 20; s.g. = 1002.
2. After ten minutes watery, clear; 2 cc.; alk. = 20.
3. After seventeen minutes light yellow, clear; 5 cc.; alk. = 25; s.g. = 1010.
4. After thirty minutes light yellow, brownish, clear; 20 cc.; alk. = 30; s.g. 1005.
5. After fifty minutes dark yellow, brown, clear; 40 min.; = 20 s.g. = 1002.

Test 11. March 19, 1921. Calomel 0.06 gm. in 60 cc. water:

1. Fasting, canary yellow, greenish tinge, turbid; 15 cc.; s.g. = 1010; alk. = 20.
2. After one minute watery, clear; 2 cc.; alk. = 15; s.g. = 1010.
3. After nine minutes light yellow, turbid; 10 cc.; alk. = 20; s.g. = 1012.
4. After eleven minutes dark yellow, clear; s.g. = 1020; alk. = 15; 40 cc.
5. After twenty-nine minutes dark brown, yellow, clear; alk. = 15; s.g. = 1010; 15 cc.

Figure 1 (J. G. B.) shows the high specific gravity after 25 per cent magnesium sulphate; the curve reached 1040, when the salt partly returns with the light bile, then in the dark bile it is 1020, in order to go down with the lighter bile to 1010.

Figure 2 (J. G. B.) gives the same items with the 13 per cent magnesium sulphate. The specific gravity in the light bile (from the admixture of the salt) gives a specific gravity of 1030, in the dark bile 1010, and goes down in the lighter bile to 1006.

Comparing figures 1 and 2 one sees the influence of the greater concentration of magnesium sulphate on the height of the color reaction (reaching up to deep brown when 25 per cent, and yellow brown when 13 per cent was given) and the specific gravity, which is correspondingly lower, with the smaller concentration.

Figure 3 (J. G. B.) shows the action of 13 per cent magnesium citrate which gives a very faint color reaction, in fact less than any of the other substances tried.

Figure 4 (J. G. B.), 5 per cent peptone, shows a good color reaction, with the specific gravity fluctuating between 1010 and 1020.

Figure 5 (J. G. B.) shows a pronounced color reaction after 8 per cent bicarbonate of soda, with the specific gravity fluctuating between 1010 and 1020.

Figure 6 (J. G. B.) shows an intense color reaction after the 25 per cent glucose, with a specific gravity between 1010-1040.

Figure 7, pilocarpine 0.005; figure 8, atropine 0.0005; figure 10, sodium chloride 0.5 per cent, and figure 11, calomel 0.06, all give good color reactions, with low specific gravities varying from 1006-1010. Figure 9, mercurochrome, give, likewise, a low specific gravity while the color reaction, although present, could not be illustrated on account of the admixture of the original red color.

With regard to the quantity of bile excreted and in what time (or length of cycle) after the different ingredients, we find the following relations in the graphs of J. G. B.:

	<i>cc.</i>	<i>minutes</i>
Magnesium sulphate, 25 per cent.....	86	60
Magnesium sulphate, 13 per cent.....	114	18
Magnesium citrate, 13 per cent.....	80	46
Peptone, 5 per cent.....	28	30
Sodium bicarbonate, 8 per cent.....	25	12
Glucose, 25 per cent.....	95	40
Pilocarpine, 0.005.....	29	25
Atropine, 0.0005.....	60	38
Mercurochrome, 0.5 per cent.....	60	50
Sodium chloride, 0.5 per cent.....	67	50
Calomel, 0.06.....	37	29

The largest amount of bile furnished was after 13 per cent magnesium sulphate, namely, 114 in eighteen minutes; the next highest is after glucose 25 per cent, 95 cc. in forty minutes.

Case 2. F. J. R., with probable cholecystitis. The following ingredients were tested:

Test 1. Twenty-five per cent magnesium sulphate, March 14, 1921:

1. Fasting, canary yellow, greenish tinge, turbid; 5 cc.; alk. = 20; s.g. = 1010; (cholesterin crystals, pus cells, and mucus).

2. After one minute watery, clear; alk. = 20; s.g. = 1010; 5 cc.

3. After three minutes light golden yellow, clear; alk. = 25; s.g. = 1020.

4. After twenty minutes very dark brown, greenish, yellow, turbid; alk. = 35; s.g. = 1030.

5. After thirty minutes shade lighter, brown, greenish yellow; alk. = 30; s.g. = 1020.

6. After forty minutes shade lighter, brown, greenish yellow; alk. = 30; s.g. = 1010.

Test 2. Thirteen per cent magnesium sulphate, March 20, 1921:

1. Fasting, light canary yellow, turbid; alk. = 20; 4 cc.

2. After ten minutes light yellow, clear, greenish tinge; s.g. = 1025; 10 cc. = 20.

3. After twenty-five minutes turbid, very dark yellow; alk. = 30; s.g. = 1020; 20 cc.

4. After thirty-five minutes light yellow, turbid; alk. = 15; s.g. = 1015; 40 cc.

Test 3. March 16, 1921. Twenty-five per cent sodium sulphate.

1. Fasting, dark yellow, greenish tinge; 5 cc.; s.g. = 1010; alk. = 20.

2. After eight minutes greyish yellow, turbid; 15 cc.; alk. = 25; s.g. = 1025.

3. After twenty minutes dark yellow, slightly turbid; 10 cc.; alk. = 20; s.g. = 1020.

4. After thirty-five minutes very dark brown, yellow, turbid; 10 cc.; alk. = 20; s.g. = 1010.

Test 4. Calomel 0.06, March 19, 1921:

1. Fasting, dark yellow, turbid; alk.; 1 cc.

2. After five minutes, watery, clear; alk. = 20; 2 cc.

3. After ten minutes light yellow, turbid; alk. = 20; 4 cc.

4. After twenty minutes dark yellow, greenish tinge, turbid; alk. = 25; 40 cc.

5. After thirty minutes light yellow, turbid; alk. = 20; 5 cc.

Test 5. One-half per cent mercurochrome, March 21, 1921.

1. Fasting, light yellow, greenish tinge, turbid; 2 cc.; alk. = 15.

2. After ten minutes dark red, clear; alk. = 15; 5 cc.

3. After twenty minutes light red, turbid; alk. = 15; 5 cc.

4. After thirty minutes canary yellow, turbid; alk. = 20; 10 cc.; s.g. = 1010.

5. After thirty-five minutes dark green, yellow, turbid; 40 cc.; alk. = 30; s.g. = 1010.

6. After fifty minutes pale red, turbid; alk. = 10; 5 cc.

Case 3. Isaac A., with gastric ulcer and chronic cholecystitis. The following ingredients were given alternately:

Test 1. Twenty-five per cent magnesium sulphate, March 3, 1921:

1. Fasting, light golden yellow, clear; alk. = 20; s.g. = 1010; 10 cc.
2. After fifteen minutes golden yellow, clear; alk. = 25; s.g. 1030; 10 cc.
3. After twenty-five minutes dark yellow, slightly turbid; 5 cc.; alk. = 25; s.g. =

1020.

4. After thirty-five minutes golden yellow, clear; alk. = 20; 10 cc.
5. After forty-five minutes dark yellow, clear; alk. = 20; s.g. 1010; 5 cc.

Test 2. Peptone, five per cent, March 5, 1921:

1. Fasting, dark yellow, turbid; alk. = 20; 10 cc.
2. After fifteen minutes dark yellow, greenish tinge, turbid; alk. = 25; 8 cc.
3. After twenty minutes dark yellow, greenish tinge; alk. = 25; 6 cc.
4. After thirty minutes canary yellow, turbid; alk. = 20; 5 cc.
5. After thirty-five minutes yellow; 5 cc.; alk. = 20.

Test 3. March 8, 1921, thirteen per cent of magnesium citrate:

1. Fasting, canary yellow, very turbid; 10 cc.; HCl = 10; Ac. = 20.
2. After twenty minutes canary yellow, turbid; 10 cc.; HCl = 10; Ac. = 20.
3. After thirty minutes light yellow, clear; alk. = 20; 10 cc.
4. After forty minutes light yellow, clear; alk. = 20; 10 cc.

Test 4. March 5, 1921, eight per cent sodium bicarbonate:

1. Fasting, dark yellow, turbid; alk. = 20; 4 cc.
2. After thirty minutes dark yellow, greenish tinge, clear; s.g. = 130; 15 cc.; alk. = 40.
3. After sixty minutes golden yellow, slightly turbid; s.g. = 1020; alk. 25; 10 cc.
4. After one and one-half hours golden yellow, turbid; s.g. = 1020; 15 cc.; alk. = 20.

5. After two hours light yellow; slightly turbid; s.g. = 1010; alk. = 20; 4 cc.

Test 5. March 1, 1921, three per cent saline:

1. Fasting, light canary yellow, turbid; 10 cc.; HCl = 5; Ac. = 10.
2. After five minutes very light yellow, turbid; HCl = 5; Ac. = 10; 10 cc.
3. After ten minutes dark yellowish, brownish tinge; alk. = 25.
4. After twelve minutes very dark brown yellow, greenish tinge, clear; alk. = 25.
5. After fifteen minutes shade darker, brownish yellow, clear; alk. = 25.

Test 6. March 11, 1921, one-half per cent saline:

1. Fasting, yellow, slightly turbid; 1006; alk. = 20; 5 cc.
2. After twenty minutes light yellow, slightly turbid; alk. = 20; 1010; 5 cc.
3. After twenty-five minutes canary yellow, turbid; HCl = 10; Ac. = 20; s.g. = 1012; 10 cc.
4. After thirty minutes light golden yellow, clear; alk. = 25; 1010; 8 cc.
5. After forty minutes canary yellow, turbid; alk. = 20; 1006; 8 cc.

Case 4. Mrs. J. L. B., patient with duodenal ulcer and probable cholecystitis. The following ingredients were tested:

Test 1. March 10, 1921, twenty-five per cent glucose:

1. Fasting, light canary yellow, turbid; alk. = 15; s.g. = 1020.
2. After ten minutes watery, clear; alk. = 15.
3. After twenty minutes light canary yellow, slightly turbid; alk. = 20; s.g. = 1040.
4. After thirty minutes very light yellow, clear; alk. = 20; s.g. = 1030.

Test 2. March 11, 1921, half per cent saline:

1. Fasting, brownish yellow, slightly turbid; s.g. = 1005; alk. = 20; 5 cc.
2. After ten minutes watery, slightly turbid; s.g. = 1004; alk. = 20; 4 cc.
3. After twenty minutes light brownish yellow, clear; alk. = 25; 10 cc.
4. After forty-five minutes brownish yellow, clear; s.g. = 1002; 40 cc.

Test 3. March 15, 1921. Pilocarpin 0.005 in 60 cc.

1. Fasting, canary yellow, turbid; s.g. = 1010; 5 cc.
2. After one minute clear, watery; s.g. = 1002; 2 cc.
3. After thirty minutes canary yellow; turbid; s.g. = 1002 = 5 cc.
4. After forty-five minutes dark yellow, brownish tinge; turbid; s.g. = 1000; 10 cc. (patient vomited).

Test 4. March 14, 1921. Atropine sulphate, 0.0005 gm. in 60 cc. of water.

1. Fasting, canary yellow, turbid; alk. = 15; s.g. = 1010; 5 cc.
2. After four minutes light canary yellow, clear; alk. = 15; 5 cc.
3. After ten minutes dark yellow, brownish tinge, clear; alk. = 15; s.g. = 1010; 5 c.c.
4. After fifteen minutes light yellow, brownish tinge, clear; alk. = 20; 10 cc.
5. After twenty minutes light yellow brownish tinge, clear; 10 cc. alk. = 20; s.g. = 1005.

Case 5. Fabian B., patient with achylia gastrica and cholecystitis. The following substances were given:

Test 1. March 25, 1921, twenty-five per cent magnesium sulphate:

1. Fasting, light yellow, turbid; alk. = 20; 4 cc. A. = 10; S. = 1; T. = 0.
2. After eight minutes light straw yellow, clear; s.g. = 1030; 5 cc.
3. After twenty minutes dark yellow, turbid; s.g. = 1030; 5 cc.
4. After fifty minutes very dark brownish green, turbid; s.g. = 1025; 40 cc.
5. After fifty-five minutes light yellow brown, clear; s.g. = 1020; 5 cc.
6. After sixty minutes light yellow brown, clear; s.g. = 1020; 3 cc.
7. After sixty-five minutes light yellow, turbid; s.g. = 1015; 5 cc.

Test 2. March 12, 1921, five per cent peptone:

1. Fasting, greyish; no bile; alk. = 10; s.g. = 1010; 15 cc.
 2. After two minutes greyish, no bile; alk. = 15; 10 cc.
 3. After four minutes dark yellow, turbid; alk. = 15; 5 cc.
 4. After thirteen minutes very dark yellow, turbid; 15 cc.; alk. = 20; s.g. = 1012.
 5. After fourteen minutes dark yellow, turbid; alk. = 20; 4 cc.
 6. After twenty-eight minutes lighter dark yellow, turbid; alk. = 20; 3 cc.
 7. After fifty minutes very dark yellow, turbid; alk. = 20; s.g. = 1010; 40 cc.
 8. After fifty-five minutes lighter dark yellow, turbid; 5 cc.; alk. = 10.
 9. After fifty-seven minutes lighter yellow; 5 cc.; alk. = 15.
- Test 3. March 19, 1921, twenty per cent. glucose:
1. Fasting, greyish turbid; alk. = 10; 2 cc.
 2. After seventeen minutes watery, clear; s.g. = 1040; alk. = 10; 50 cc.
 3. After forty minutes dark yellow, turbid; 1020; alk. = 20; 20 cc.
 4. After fifty minutes shade lighter yellow, turbid; alk. = 25; 15 cc.
 5. After fifty-six minutes greyish, turbid; alk. = 10; 10 cc.

A number of other patients were given the different salts mentioned and also various medicaments. The present article would become too cumbersome should they all be described. Suffice it to say that similar reactions although in various graduations, were obtained in most patients from all the ingredients tested. The specific gravity of the dark bile was increased, when the substance given had a high specific gravity (magnesium sulphate, glucose) and not increased when the substances ingested did not influence it, like peptone, calomel, atropine, pilocarpine, etc.

Four new cases, patients with cholecystectomies, Mrs. B. G., Miss M. L., Mrs. C. S., and Mrs. Y. S., gave a good reaction with magnesium sulphate and also with 5 per cent peptone solution. Studies of 2 of these cases, Mrs. B. G. and Miss M. L., are illustrated in graphs 12 to 15. Here also as in patients with the presence of a gall-bladder the specific gravity of the dark bile after magnesium sulphate is much higher than in the dark specimen obtained after the peptone instillation. In fact all the substances producing reaction (dark bile) do it whether the gall-bladder is present or not. It is evident that the gall-bladder as such has nothing whatever to do with this phenomenon.

Dr. Willy Meyer and I were able to furnish another positive proof that the dark bile need not come from the gall-bladder, but can be eliminated from the liver directly. The following instance demonstrated this very clearly:

Patient H. B. with cholecystitis, was given magnesium sulphate on the day previous to operation. He gave a characteristic dark bile reaction as the following notes from our notebook demonstrated and as the subjoined graph (16) shows:

Case. 6. Mr. H. B., with chronic cholecystitis; March 21, 1921; 25 per cent magnesium sulphate.

1. Fasting, pea soup appearance, yellow turbid; alk. = 10; 20 cc.
2. After five minutes dark yellow brown, greenish tinge, turbid; 40 cc.; alk. = 20; s.g. = 1050.
3. After ten minutes brownish yellow, turbid; 10 cc.; HCL = 10; Ac. 20; s.g. = 1040.
4. After twenty-one minutes dark brown yellow, greenish tinge; 40 cc.; s.g. = 1030; HCL = 5; Ac. = 10.
5. After twenty-six minutes yellowish green on upper three-quarter; dark brown yellow on lower one-quarter; 40 cc.; s.g. = 1020; alk. = 20.
6. After thirty minutes greenish yellow, turbid; 10 cc.; alk. = 25; s.g. 1010.
7. After forty minutes light yellow, brown, turbid; alk. = 20; s.g. = 1010; 10 cc.

H. B., March 23, 1921, twenty-five per cent magnesium sulphate during operation:

1. Fasting, light yellow, very turbid; alk. = 20.
2. After eleven minutes light yellow, greenish tinge, turbid; alk. = 35; s.g. 1016.
3. After thirty minutes light greenish yellow, slightly turbid; s.g. = 1060; alk. = 30.

At the operation (the duodenal tube had been left in situ) two important points were ascertained: (a) magnesium sulphate was given through the tube; after waiting from five to ten minutes no dark bile was obtained. The gall-bladder which was exposed and constantly observed did not show any contractions; (b) at the operation the cystic duct was found tightly closed by a stone so that nothing could leave or enter the gall-bladder. Moreover, after opening the latter, the contents were found to have a reddish appearance and consisting of pus and red blood corpuscles mixed with mucus, without any bile.

Inasmuch as there has been no bile in the gall-bladder and this condition must have existed for quite some time and inasmuch as nothing could enter or leave the vesicular cavity, the dark file obtained the day previous could not have originated from this source and must of necessity have come from the liver ducts (choledochus).

In a few rare instances the color reaction of the bile after magnesium sulphate appears quite abruptly, lasts a little while and suddenly ceases. In these cases it would be natural to assume that the dark colored bile came from the gall-bladder as a result of the relaxing action of the magnesium salt. This, however, does not seem to be the case, for in these patients other salts, especially bicarbonate of soda, or other liver irritants will do the same, showing that this phenomenon is not due to an evacuation of the gall-bladder contents. As an illustration the following two graphs are given:

Case 7. John G. R., patient with duodenal ulcer and chronic cholecystitis.

Test 1. March 23, 1921. Twenty-five per cent magnesium sulphate.

1. Fasting, watery, canary yellow, turbid; 5 cc.; s.g. = 1010; alk. = 15.
2. After five minutes yellow, watery; s.g. = 1010; 5 cc.
3. After ten minutes light yellow, greenish tinge, turbid; alk. = 30; s.g. = 1035; 15 cc.
4. After twenty-five minutes very dark brown, turbid; alk. = 40; s.g. = 1035; 40 cc.
5. After thirty-five minutes light brown, turbid; alk. = 30; s.g. = 1020; 15 cc.
6. After forty minutes very light yellow, brownish tinge, slightly turbid; alk. = 25; s.g. = 1015; 5 cc.
7. After forty-five minutes light yellow, slightly turbid; alk. = 20; s.g. = 1015; 15 cc.

Test 2. March 28, 1921. Eight per cent bicarbonate of soda:

1. Fasting, very light yellow, turbid; 20 cc.; HCL = 10; Ac. = 20.
2. After ten minutes light yellow, clear; s.g. = 1040; alk. = 20; 40 cc.
3. After twenty minutes dark yellow, slightly turbid; alk. = 30; s.g. = 1020; 15 cc.
4. After thirty minutes light yellow, clear; alk. = 15; s.g. = 1020; 15 cc.
5. After forty minutes light yellow, clear; alk. = 10; 4 cc.

The difference in the specific gravity of the dark bile after magnesium sulphate and that after the bicarbonate of soda clearly indicates that this process is not due to a mere release of concentrated bile from the bladder, but rather to a chemical action on the liver. Thus the higher concentration of the magnesium salt (25 per cent) caused an elimination of a bile of a higher specific gravity than bicarbonate of soda (8 to 9 per cent).

From my experiences with different salts and other chemical ingredients when injected into the duodenum, it is apparent that the liver can be induced to a greater activity to an elimination of a darker, more concentrated bile.

As mentioned in my former paper on this subject, injections of these substances into the duodenum can be conveniently used as a functional test of the activity of the liver. Magnesium sulphate, sodium sulphate, peptone, glucose solutions, also bicarbonate of sodium, appear to be appropriate for this purpose.

We give here 3 new cases of severe liver lesions in which this color reaction of the bile after the injection of these liver stimulants into the duodenum did not show up. One of these cases is given in graph 19. The others are briefly described.

Case 8. S., patient with cancer of the liver.

Test 1. January 21, 1921. Twenty-five per cent magnesium sulphate.

1. Fasting, dark yellow, turbid; 5 cc.; alk. = 15.
2. After eight minutes dark yellow, clear; alk. = 30; s.g. = 1050; 15 cc.
3. After thirteen minutes dark yellow, turbid; alk. = 20; 5 cc.
4. After eighteen minutes dark yellow, turbid; alk. = 20; s.g. = 1020; 40 cc.
5. After thirty-three minutes very dark yellow, turbid; s. g. = 1015; alk. = 15; 40 cc.

Case 9. Mrs. A. A.; January 18, 1921; patient with subnutrition and chronic cholecystitis.

Test 1. Twenty-five per cent magnesium sulphate:

1. Fasting, dark yellow, turbid; alk. = 15; 5 cc.
2. After five minutes light yellow, clear; alk. = 15; 5 cc.
3. After eleven minutes light yellow, slightly turbid; alk. = 20; 5 cc.
4. After twenty-one minutes dark yellow, turbid; alk. = 20; s.g. = 1030; 15 cc.

5. After forty-three minutes shade lighter yellow, turbid; alk. = 20; 10 cc.

6. After fifty-two minutes dark yellow, clear; alk. = 20; 4 cc.

Test 2. Mrs. A. January 1-15-19-21. Twenty-five per cent sodium sulphate:

1. Fasting, dark yellow, greenish tinge; alk. = 16; 10 cc.

2. After three minutes light golden yellow, turbid; alk. = 15; 5 cc.

3. After eleven minutes light golden yellow, turbid; alk. = 20; 10 cc.

4. After seventeen minutes light golden yellow, turbid; alk. = 15; 10 cc.

5. After twenty minutes yellow, turbid; HCl = 5; Ac. = 10; 5 cc.

6. After twenty-eight minutes light golden yellow, turbid; alk. = 10; 5 cc.

7. After thirty-five minutes dark yellow, slightly turbid; alk. = 15; 5 cc.

Test 3. 1-22-21. Twenty per cent glucose:

1. Fasting, light yellow, turbid; alk. = 15; 3 cc.

2. After five minutes light yellow, turbid; alk. = 20; 5 cc.; s. g. = 1060.

3. After ten minutes light yellow, turbid; s. g. = 1045; alk. = 20; 10 cc.

4. After twenty minutes light yellow, clear; s. g. = 1030; alk. = 15; 5 cc.

Case 10. Mrs. Anna R., with cholecystitis and cirrhosis of the liver (with jaundice); March 21, 1921. Twenty-five per cent magnesium sulphate.

Test 1. Fasting, greyish, tinge of yellow, turbid; alk. = 10; 2 cc.

2. After eight minutes light yellow, clear; alk. = 10; 5 cc.

3. After ten minutes light greenish yellow, slightly turbid; alk. = 20; s. g. = 1024; 40 cc.

4. After forty minutes yellowish, greenish tinge, turbid; alk. = 20; s. g. = s. g. = 1025; 40 cc.

Test 2. March 28, 1921. Eight per cent sodium bicarbonate. 3-28-21:

1. Fasting, light green yellow, clear; alk. = 10; 10 cc.

2. After ten minutes light green yellow, clear alk. = 20; 20 cc.

3. After fifteen minutes dark green yellow, clear; alk. = 20; 30 cc.

Lyon had suggested to employ the magnesium sulphate instillation as a diagnostic means of gall-bladder lesions and also for the differentiation of the different biles (from gall-bladder, common duct, and hepatic duct).

As shown before and in this paper again Lyon's assumption of the different sources of bile, as judged by the color, does not seem to be correct.

The question arises what are the best conditions for the examination of the bile in gall-bladder lesions.

Inasmuch as the magnesium sulphate and other liver stimulants increase the flow of bile from the liver and drive it, so to say, quickly and directly into the duodenum, there will be after these substances a bile product from the liver direct containing very little if any bile from the gall-bladder. In the fasting condition and without any previous stimulation the aspiration succeeds in obtaining what little bile there is in the duodenum from the liver and the gall-bladder, or

there seems to be more chance for the appearance of some gall-bladder bile when the flow of liver bile is not extensive.

In practicing the bile examinations in the fasting state of the patient for the last ten years or so, I found this to be the case.

Diagnostically then we can find many more valuable hints regarding gall-bladder lesions from the examination of the natural fasting bile than from the bile obtained after the stimulation by magnesium sulphate.

In cases of jaundice, however, in which no bile is found in the fasting state, a liver stimulant may be injected into the duodenum, in order to ascertain whether the increased flow of bile from the liver is still able to push through some of its products into the duodenum. In fact, in a number of such cases of chronic jaundice with no bile in the duodenum while fasting, the magnesium sulphate caused the appearance of some bile after a short time, thus showing that the common duct occlusion was not complete. In these cases the magnesium sulphate or peptone or glucose test is of diagnostic aid.

Before I conclude this paper I wish to thank Dr. Willy Meyer and Dr. Torek for permission to examine their cases and Dr. H. Bockus, Dr. H. Puhlman and Dr. H. A. Rafsky for assisting in carrying out the investigations.

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DISCUSSION

DR. B. B. VINCENT LYON, Philadelphia: I presume that it would be perfectly natural that I would want to discuss this paper. I also feel that it is right to make the statement that the work in which I am personally engaged in this field of possible investigation is now a little over four years old. I have passed my four hundred and fiftieth personally handled case with something over 4000 biliary drainages on those cases. I have also passed on the records or on some of the findings or I have had something to do with the way of controlling the examination in probably a like number, if not a large number, of examinations done by clinical assistants or for other doctors who were interested to have me look at their findings. I can say now that I do not believe that if I were re-writing any of the papers that I have already written that I would care to change them in any material detail with the exception of one which I may have a chance to refer to. I am quite familiar with the publication which Dr. Einhorn brought out in February last. In fact a great many months before the publication of that paper I had gone through a series of observations on each of the chemicals that he has used—sodium phosphate, magnesium sulphate, peptone, etc., and in addition to them I have gone over a large number of the

chologogic group of medicines for the purpose of comparing their effects with those obtained from magnesium sulphate in the hope of finding something that was better than magnesium sulphate for the purpose. But up to the present I have found nothing nearly so good as Epsom salts. If I were a lawyer instead of a doctor and familiar with both sides of the argument in preparing the case, I think I could take Dr. Einhorn's paper and make it a better brief for the substantiation of the method which I have outlined than to use it for an antagonistic line of reasoning. I believe that Dr. Einhorn has misinterpreted his findings, although I am quite prepared to admit that I may have misinterpreted my own. The only thing I welcome is the greatest amount of free discussion, but I think it would be a wise matter to wait until one has accumulated a large series of cases, because a number of the points that I have brought out do not appear in the review of a few cases; it is only by the frequent repetition of the same type of finding that we begin to be impressed with the merits of the method. We should remember that a negative microscopic or cultural finding in any case of suspected biliary tract disease is to be given only the same value as a negative finding for tubercle bacilli in a clinically positive case of pulmonary tuberculosis, etc.

I would like to take up some of the points which Dr. Einhorn has made. He says the change of the color to a dark bile may not be abrupt. As a rule, it is not abrupt, but in a great many instances it may be very abrupt and this may depend a great deal upon whether or not the ampullic sphincter (illustrated by drawing) at the duodenum is closed or open. If this duct is found open before you stimulate the duodenum with the instillation of 33 per cent magnesium sulphate, naturally your bile within the common duct has escaped, and therefore one cannot in this case segregate properly the three types of bile. Here then the bile that one usually gets is bile trickling down the right and left hepatics with a gradual mixture of bile coming from the gall-bladder, so that it may be a few moments before one gets a transition to the deeper-colored bile, but in a great many instances, and I am sure that those who have had a long experience with this have encountered them, occasionally it is noticeable that there is a sudden gush of very dark bile immediately after bile of any type is obtainable. In these cases we may presume that the gall-bladder wall is under tension.

Now as to the alterations in flow; that is, the alteration in color of the bile may go from a dark to a light yellow and back again to a dark bile. This is often perfectly interpretable. A great many gall-bladders, provided there is no obstruction in the cystic duct, may have a weakened or atonic musculature so that they are incapable of emptying themselves at a single contraction, but do so only under repeated stimulation. We do not know; we have never actually seen in contract, but it is possible that all its bile may not be ejaculated at a single contraction, and therefore the very thing that Dr. Einhorn brings up as his strongest point that on apparently emptying a gall-bladder and then restimulating he often gets more of this dark bile, means that he is really using my method of repeated fractional stimulations with magnesium sulphate in order to more completely empty the atonic gall-bladder.

I can only recommend that a review of Dr. Einhorn's paper may be carried on by any individual who may be interested enough in the general subject to do so.

I will just outline my personal reasons for believing that this darker bile is derived in large part from the gall-bladder without enlarging upon them. First,

because in these thousands of drainages which I have personally seen, the normal sequence in normal cases and in my classified pathological cases is almost always the same. I do not mean identically the same, but in general they run a very similar drainage process. Second, the usual sequence of events in pathological cases with the gall-bladder still in the body usually runs much the same type of drainage with various alterations in the character of the bile from the gall-bladder, ducts or liver, depending upon the nature of the pathological process present. Third, the usual sequence of events in both normal and pathological cases in which the gall-bladder has been removed is usually of the same type. In other words, in our cholecystectomized cases we do not recover any of the normal darker colored bile, unless there is some post-operative complication or sequela, such as a continued infection or catarrh within the ducts causing a partial obstruction with a certain amount of resultant dilatation of the ducts, but even with this we never encounter the very deep green-black biles of the pathological static-gall-bladder. Occasionally, however, we do recover a darker bile that may simulate that from the normal gall-bladder, but this occurs usually in cases in which the common duct post-operatively dilates or in cases in which there is a tendency to a development of a diverticulum at the stump of the cystic duct (perhaps nature's attempt at the reformation of a gall-bladder), and, finally, in certain cases in which the finer biliary radicals are dilated well up into the substance of the liver and a darker bile is being delivered from this perilobular duct system due to stasis around the liver lobules, or, in other words, in cases in which a biliary cirrhosis has already developed.

The fourth reason for my belief that this dark bile is gall-bladder bile, and not due to chemical changes following the instillation of the magnesium sulphate, is because we have repeatedly proved that in those cases in which the gall-bladder has not been removed, and in whom we fail to recover gall-bladder bile at post-operative check up, it has been found due to obstruction of the cystic duct from several causes, such as stone, adhesions, pressure from without, inflammatory edema and catarrh from within, inspissated bile, or to atonic gall-bladders incapable of delivering their contents. In many instances since we have learned these points we have, by persisting in treatment, been able to clear up a cystic duct obstruction if due to catarrh or inflammatory edema, as later demonstrated by our final recovery of typical dark gall-bladder bile checked up by the microscopical recovery of spiral strands of dense mucus studded over with amorphous bile salts, pus cells and inflammatory debris, and coincident symptomatic recovery of the patient.

Finally, if "B" bile is not being derived from the gall-bladder, how else can we so well account for our recovery of small gall stones or gall sand directly through the tube, or our recovery of larger stones found in the sieved stools of patients who have recently had duodeno-biliary drainage? How else can we so well account for the reproduction of gall-bladder pain, either of a definite colic type, or a sense of upper right quadrant soreness, or of infrascapular pain (due to adhesions), following certain of our drainages in cases with definitely inflamed and infected gall-bladders? How else can we account for our recovery of practically pure pus in several of our proved cases of operated empyema of the gall-bladder? How else can we so well account for not only the symptomatic recovery, often brilliant, of a very large series of patients after a course of non-surgical biliary drainage, but also for the coincident improvement in, or final disappearance of, the pathological objective microscopical and cultural findings in such patients?

Therefore, I contend that Dr. Einhorn's explanation of these various phenomena as being due to chemical changes taking place within the liver or gall tract as the result of the duodenal instillation of magnesium sulphate is not correct, and until better explanatory facts can be brought out I shall continue to rest my case on this platform.

DR. CHESTER M. JONES, Boston: I appreciate the honor of being allowed to make a few remarks. I hesitated in beginning in the view of Dr. Einhorn's very splendid paper and large clinical experience. We have run through a large series of cases at the Massachusetts General Hospital this year, the observations on which may be of interest in this relation. I may say that I read Dr. Einhorn's paper that came out in February, and the curves that we obtained by fractional analysis of the duodenal contents show the same results as he obtained. They show a curve, (illustrating by drawing) magnesium sulphate being given at this point. The estimation instead of being made by direct viewing of the color was made by spectroscopic examination of the pigments. We took fractions at fifty-minute intervals at an hour and a half before and after administration of magnesium sulphate. Now in a large series of cases of pernicious anemia, hemolytic jaundice, etc., we always obtained this type of curve (drawing). The height of the curve was different in different cases. The cases that did not show this type of curve I think are interesting and they do not correspond with the results of Dr. Einhorn. Our cases were cases which showed stone at the cystic duct, occluding the flow; the others were after cholecystectomy so that no bile from the gall-bladder could enter the duodenum. Careful estimation showed that sort of curve in the case (drawing). There was a rise in value obtained after the administration of magnesium sulphate. We attributed that to a better flow obtained, possibly to the relaxation, but in no case was there anywhere near as high a peak in the entire series with these exceptions. Furthermore in sediments in a series of gall-bladder cases studied show characteristic findings which were confirmed by operation and mean a characteristic finding of cellular elements and crystalline elements which appeared not in the duodenal contents but in the gall-bladders at operation. The interesting point is that the fractions that showed those were obtained at this point (showing); in other words, at the point where the pigment curve was high.

We did not try any other salt besides magnesium sulphate. We had occasion to observe that the administration of hot water produced a curve comparable in all respects to this curve here; and we attributed that to a relaxation of the duodenum and a better flow of bile into the duodenum.

In a series of pernicious anemia cases these show instead of this typical curve here an immediate rise to that level before the giving of magnesium sulphate and then that was given and the peak did not go higher and gradually fell off. Those cases were those in which a particularly free flow of bile was noticed throughout the examination.

One more case was a case in which we took fractional readings over a period of five to six hours. We did the case twice. In both experiments this type of curve was obtained after magnesium sulphate, reaching a peak of this level. An hour later magnesium sulphate was given again, and a similar curve was obtained. However quantitative estimation of the pigment did not show so high a peak, and an hour later it came down, and we were unable to obtain more than a minimal rise following the use of magnesium sulphate.

I merely offer these observations for the practical interest in these cases, and I should be glad to hear Dr. Einhorn's explanation.

DR. WILLY MEYER, New York: I hope there are no objections to the surgeon participating in this most interesting and important discussion. Naturally, these investigations as such must be left to the specialist and internist. And yet, in view of the condition of borderline work of today, it not only interests the surgeon greatly from a scientific point of view, but affects him in his work directly.

Permit me to say from the start that, to my mind, Dr. Lyon deserves great credit for having taken up this question and for having further instilled into the profession the stimulus of investigating the duodenal contents on broad lines. I believe there is hardly a hospital of standing in the United States today that is not investigating this very question. Particularly can one observe, that almost every medical division, but also of the surgical and of the specialties. Today we know as a fact that the instillation of the 25 per cent solution of magnesium sulphate into the duodenum as introduced by Dr. Lyon in regard to the efficient treatment of catarrhal jaundice has had remarkable curative results. We are further hopeful that the use of magnesium sulphate will have great benefit in the after treatment of cholecystectomy, when paroxysmal attacks of pain, most probably due to a subacute or chronic cholangitis, persist. The treatment of the latter by operation gives little promise for good results. Even prolonged drainage of the common or hepatic duct after cholecystectomy will but rarely cure cholangitis.

Having stated these facts, let us enter the question at issue with an open mind. I am convinced that both gentlemen, who have just spoken, have an open mind. But do not let us forget that we are just at the threshold of this new chapter. Let me discuss just a few points. When many of us listened with intense interest to Dr. Lyon's presentation of his procedure at the meeting at Atlantic City last year I must say that it struck me at once as a remarkable occurrence that the amount of bile Dr. Lyon claimed to have been discharged from the gall-bladder was such a large one. I then said to myself: that must have been a gall-bladder of tremendous size which contained this amount of fluid; it was at least 8 or 10 ounces. Furthermore, it has always struck me as most peculiar that with this so-called Meltzer-Lyon test with magnesium sulphate, or also with sodium, pilocarpine, etc., we always get the same color of the bile drained into the duodenum, *black*, while if we aspirate the viscus during the operation just before we extirpate the gall-bladder we find all kinds of shades, greenish, greenish-black, mirky, yellow, etc. We also made use of the time during the operation for watching what the gall-bladder is doing after the instillation. In several instances we left the duodenal tube in situ, did not place any gauze pads within the peritoneal cavity and then injected the twenty-five per cent solution of magnesium sulphate into the duodenum. And not only the surgeon, but everybody busy at and interested in the operation watched. But not the slightest contraction of the gall-bladder was ever observed. Of course, it is admitted that this experiment is not quite correct. In the way Dr. Lyon advised to do the work, the abdominal cavity is closed, and here it is open. The atmospheric pressure, freely admitted to the intra-abdominal organs, may change the value of the experiment.

But the fact, that, after this duodenal instillation of various chemicals dissolved in water, we always observe the same color of the discharged bile—black, black,

black,—while the aspirating needle finds different shades of bile within the bladder, and the further fact that we could never notice a contraction of the gall-bladder while making the test in the course of the operation, made me think a great deal and accept as correct Dr. Einhorn's conclusions, that this black, so-called "B" bile is not discharged from the gall-bladder, but represents principally a product of the liver. It is, of course, self-understood that the contents of the gall-bladder are also discharged, in part or completely, during the test and get mixed with the "B" bile, but the "B" bile certainly does not represent the gall-bladder contents alone. I have, therefore, on my division, given up using the magnesium sulphate instillations into the duodenum for diagnostic purposes. The method has value in the therapy, but not in the diagnosis of gall-bladder disease.

Dr. Lyon's belief, as just stated by him, that the same black fluid might be expressed from a newly formed gall-bladder if found in this test after cholecystectomy, cannot be corroborated by actual fact. When performing cholecystectomy I always proceed from the fundus toward the cystic duct. I expose most carefully the junction of common and cystic duct and place the ligature right close to the ductus choledochus; nature has there no possible chance of forming a new gall-bladder, as some surgeons claim to have seen. Dr. Einhorn also repeated his test in patients, operated upon by me in this way, as early as two weeks after the operation, nevertheless, the same phenomenon, a black bile, was obtained, perhaps not quite as pronouncedly black as it was before the gall bladder was removed, but just the same "black."

For the patient, as well as for the surgeon, these preliminary investigations have done a tremendous amount of good. In the presence of recurring abdominal pains in the lower and upper abdomen and of turbidity and pathology of the duodenal contents obtained in the fasting condition of the patient previous to the surgeon's work, we do not cut down any more on the appendix, as formerly done by the majority of surgeons, then put in our hand and palpate the gall-bladder in order to feel whether there are stones present or not, but we cut down on the gall-bladder primarily and then lift the appendix into the wound and remove it. We can then inspect the gall-bladder with its surroundings, and also all the organs in the upper abdomen; we can see and investigate adhesions present, etc., and make up our mind what is best to do for the patient.

From what I have seen, I believe that chronic cholecystitis without stones is a very frequent disease, that it takes the same place in the upper abdomen as chronic appendicitis does in the lower abdomen. According to our present views the gall-bladder, if chronically inflamed, with or without stones, has to come out, should the patient desire to be cured of his trouble.

DR. MAX EINHORN, New York (closing): I would answer Dr. Jones—in regard to the curves the way I have made them—first we do not get the same curve in all. Some people have a very dark color, others not; but in most of them I do not get them at just one point. The way I get them is not in that way.

With regard to Dr. Lyon's discussion—that point which Dr. Lyon mentioned that in some there is an abrupt change of color and that is correct. True, I mentioned it in my paper. If I had such a patient, I would say that here probably the gall-bladder emptied itself. What shall we do? I gave in place of magnesium sulphate

bicarbonate of soda, 80 cc. I got again an abrupt change in the color after the bicarbonate of soda and a little less color but dark too, showing that it is not the gall-bladder but it is the action of these salts upon the liver, and that some people react differently. In some people it comes in a stream, so to speak and in others it comes gradually. Why it is, I do not know.

Then there is another point of importance—in some cases of real gall-bladder trouble where there is pus in the gall-bladder we find in the fasting condition a bile that is turbid, contains pus corpuscles, cholesterin crystals, bacteria, etc., we give the magnesium sulphate, and what do we see? The dark specimens are clear, they contain nothing. What does it show? That the dark specimens do not come from the gall-bladder.

SOME ADVANTAGES AND DIFFICULTIES OF NON-SURGICAL BILIARY TRACT DRAINAGE

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The Meltzer-Lyon method of drainage of the bile passages by means of the duodenal tube and douching the duodenum with a magnesium sulphate solution has attracted much attention and is being tried at the present time in many medical and surgical clinics throughout the country and within a year to two, we shall have a large amount of data which will definitely settle the value of the method in diagnosis and treatment of diseases of the liver and biliary passages. The method has aroused much interest and some enthusiasm over the prospect of better diagnosis and treatment and has met with much skepticism as to the possibility of telling where the bile comes from or of draining the gall-bladder in this way or of culturing its bacteria. In introducing a new method, it is natural to stress its good points and to say less about its difficulties and limitations. This tone is easily heard in the earlier papers.

My own experience with the method covers nearly a year and about 100 cases and I prefer at this time, to give my general impressions of the method rather than an elaborate statistical study. There are many phases of the subject, physiological, chemical, bacteriological and clinical which need further study and I realize, in looking backward, that data in the earlier cases was incomplete.

The appeal of the method is very strong both to doctor and patient. The doctor has the contents of the bile passages in his hands after a simple procedure and can examine it in any way he chooses, chemically or for cells and bacteria. There is also the appeal of early diagnosis and early preventive treatment before real damage has been done to the liver and bile passages. The "bilious" patient sees his bile taken out of him and feels that he is cleaned out and something nasty is being taken away.

There is much that is easy and simple about the method. It is easy to get patients to submit to it. The hope of a better diagnosis and perhaps of a medical cure is attractive.

It is usually easy to get the tube in. The statistics in 100 consecutive ambulatory cases examined at my office in which the position of the tip of the tube was verified by the fluoroscope, showed that 80 were well placed in the duodenum in twenty to thirty minutes, 15 required from thirty minutes to one hour, 1, two hours and 4 failed to pass (adhesions, atonic stomach, vomiting of tube, etc.). These figures represent the milder or moderate grade of ambulatory cases. The per cent of delayed passage and of failures to intube will be higher in the sicker or ward patients, in those with extensive adhesions or with deep jaundice and nausea, so that the failures to pass the tube to the duodenum may reach 10 per cent or even more.

It is easy to get the bile out. Anyone can do it, a nurse or attendant or even the patient himself after a few lessons.

On the other hand, there is much that is *not* so easy about the method. It is not easy to tell just where the bile comes from or why it flows so freely, whether as a result of relaxing the common duct sphincter, or of stimulation of the liver or both. It is not easy, at present, to definitely explain the color changes in the bile, whether due to emptying the gall-bladder of darker bile or to a change in liver secretion after magnesium sulphate. It is not easy to decide about the cells one sees, whether they come from inside the bile passages or from outside (stomach, bowel, etc.). It is not easy to interpret the cultures and to decide whether they are important causative bacteria or extraneous contamination. It is not easy to sum up the diagnostic value of the method, especially if one has a large series of cases with few operations.

We will discuss these things separately as far as time permits.

PHYSIOLOGY

Certain facts have been observed after local douching of the duodenum with $MgSO_4$ solutions and aspiration of the bile through a duodenal tube which have been interpreted in various ways by different men. After this use of magnesium sulphate in normal and many sick persons, a free flow of bile occurs, usually light yellow at first, later changing to darker or brownish yellow and later still to light yellow again. Lyon's theory is that the first pale yellow or "A" bile comes from the common duct, that the second darker more viscid "B" bile comes wholly or largely from the gall-bladder and the third clear yellow, thinner "C" bile is freshly secreted liver bile and that he is able, in this way, to obtain the bile *separately* from common duct, gall-

bladder and liver and establish a refined diagnosis of the different sections of the biliary system.

The method of Lyon is based on the facts that there is a loose sort of sphincter discovered by Oddi at the lower end of the common bile duct at the papilla of Vater which has a definite sphincteric action and on the discovery by Meltzer that magnesium sulphate applied locally relaxes this sphincter and permits a flow of bile into the duodenum. This is very important as by means of this relaxation, we are able to drain the bile passages. Simultaneous, forcible contraction of the gall-bladder at the same time after using magnesium sulphate has not been proved, I believe, by any laboratory experiment. Doyon has found a double or crossed innervation to the gall-bladder and ducts so that stimulation of the *central* end of the vagus (or of the *peripheral* end of the splanchnic nerves) causes simultaneously a relaxation of Oddi's sphincter and a contraction of the gall-bladder. This emptying of the gall-bladder is covered by Meltzer's "law" of contrary innervation." This "law" may apply *after the use of magnesium sulphate* in this field and probably does, but we have no definite proof thus far. The gall-bladder is a rather inactive limp affair with little muscle fiber and we are forcing the comparison a little when we compare it to the muscular urinary bladder. Even if the normal gall-bladder does contract after stimulation with magnesium sulphate, the thickened rigid fibrous, adherent, pathological ones do not.

On the other hand, *the bile does flow, it flows freely, it is an every day experience, it is absolutely unquestioned.*

The emptying of the bile passages when the sphincter is relaxed is probably due to siphonage or running out of the bile and perhaps more or less to contraction of the gall-bladder.

It has been found that with the gall-bladder exposed during anesthesia and then stimulated by magnesium sulphate, the gall-bladder did not visibly contract; but these experiments may be vitiated by the effect of the anesthetic on the muscle fibers of the gall-bladder. On the other hand, Sachs has several times at operation seen the distended gall-bladder gradually collapse and empty through the duodenal tube after the use of magnesium sulphate. He compares this to the collapse of a balloon when the air is let out, no muscular *contraction* was observed.

The bile flow and color found after the use of magnesium sulphate is explained by Einhorn and Dunn and Connell is quite another way.

Einhorn does not believe that the darker bile is gall-bladder bile necessarily but that it is due to the effect of the MgSO_4 as a liver stimulant, increasing the flow of bile directly from the liver and driving it rapidly and directly into the duodenum. He finds that the stronger the MgSO_4 used, the darker the bile and the higher its specific gravity. He finds that other salts such as sodium sulphate and sodium bicarbonate with no relaxing action on the duct sphincter, give a similar color reaction to MgSO_4 and that a group of patients without gall-bladders (cholecystectomy) give a similar color reaction; that all substances producing dark bile do it whether the gall-bladder is present or not. In short, he does not believe that the color change is due to the emptying of gall-bladder contents.

Dunn and Connell have made some interesting experiments on bile flow after introducing Mg into the duodenum in a patient without gall-bladder or common duct and in whom the hepatic duct has been anastomosed to the duodenum and who had also a duodenal fistula. Here was no sphincter of Oddi to be relaxed and no gall-bladder to be emptied. The patient's digestion was good and she felt well during the entire period of the studies. The typical "A", "B", "C" sequence of colored biles was obtained. The same result was obtained when MgSO_4 was injected into the duodenum, 32 cm. below the second part of the duodenum and also when the MgSO_4 was taken by mouth. Quantitative studies of the bile showed that the color changes were due to a variation in the amount of bile pigments present. They conclude that the color changes in the bile are due to a reaction of the liver to the presence of magnesium in the portal blood after absorption from the bowel.

To sum up, we may say that all observers agree that there is a free flow of bile, a free "drainage" of the unobstructed biliary system after the use of MgSO_4 with the appearance of a more concentrated, darker bile containing more bile pigments, although they explain this result in different ways, one by relaxing the common duct sphincter and contracting the gall-bladder and the other by stimulating an increased flow of bile from the liver. *The practical point is that it is possible to empty the bile passages more or less completely at will by the use of MgSO_4 and that this material is well worthy of study, however it is obtained.*

Lyon's theory that bile from different parts of the biliary tract, common duct, gall-bladder and liver, can be judged largely by the gross color, needs further proof before it can be accepted without reservation as a method of *localizing* disease in the biliary passages.

How complete is the emptying of the gall-bladder in this method? This is, of course, important in treatment. Unfortunately, we do not know. My impression is that it varies a good deal in different cases even without gross obstruction and in the same case at different times. This may lessen the value of the method both for diagnosis and treatment or require repeated stimulation and prolonged drainage as emphasized by Smithies.

GENERAL TECHNIQUE OF THE METHOD

This has already been much described by Lyon, Smithies, Simon, Friedenwald, Sachs and others, but it may be well to run over it briefly as it is new to many.

The patient is examined fasting (and for this reason usually in the morning). This is very important as it takes little mixed food to block the small tube and delay the washing out of the stomach. The teeth are well brushed and the mouth thoroughly rinsed with liquor antisepticus. The patient sits down and a sterile duodenal tube with Rehfuß or Lyons tip is passed into the stomach and the fasting residue is aspirated with a syringe and examined as desired (HCl, blood, cells, bacteria). The stomach is then thoroughly washed with a weak zinc chloride formalin solution¹ running in about 300 cc. at a time and syphoning it out again till the washings are absolutely clear (this takes about twenty minutes). The patient now lies on a couch with head and shoulder slightly raised, turned about halfway toward the right side and swallows the tube *slowly* to the 75 cm. mark, taking about twenty minutes to do this. Sometimes, a few ounces of water are sipped to help the progress of the tube. When the tube is in the duodenum (see below) the duodenal contents are aspirated with a syringe and then the duodenum is douched with a one-third saturated solution of magnesium sulphate in water (30 cc. of saturated solution of $MgSO_4$ in water, mixed with 60 cc. of water). The plunger of the syringe is removed and the $MgSO_4$ solution is poured into the barrel of the syringe attached to the tube. The tube is then attached to a 6-ounce aspirating bottle with rubber cork and two

¹ The stock solution is:

Formalin	0.5 gram
Zinc chloride	2.0 grams
Boric acid	10.0 grams
Water	1000 cc.

We use 25 cc. in 250 cc. water for lavage.

openings, one connected with a small rubber aspirating bulb. Gentle aspiration is begun at once and the bile soon starts to flow and continues with little or no help from the aspirator. Lyon separates three types of bile during this flow chiefly by color and consistency. In normal cases, the first or "A" bile is light, golden yellow and rather thin, the second or "B" bile is darker yellow and more ropy, the third or "C" bile is light yellow and thin. Lyon considers that "A" represents bile from the common duct, "B" from the gall-bladder and "C" from the liver and hepatic ducts.

The biles are collected in separate sterile bottles for examination. The color must be noted when fresh as most biles soon darken on standing. The cells also must be examined at once as they are readily digested by ferments present.

The drainage usually takes from twenty to thirty minutes and about 15 or 20 cc. of "A" and 50 or 60 cc. of "B" and "C" bile obtained. When this is finished, the duodenum is douched with 300 cc. of normal salt or Ringer's solution and the tube withdrawn. The bowels are usually moved more or less freely by the $MgSO_4$ solution which is considered desirable, as it may carry infected bile out of the lower bowel. A light lunch of malted milk or broth and crackers is given after the drainage to avoid weakness.

Several of the steps in the process will be considered separately.

THE PASSAGE OF THE DUODENAL TUBE

The early methods of introducing the tube were slow, taking one to two hours or often overnight. With the rapidly growing use of the tube, a rapid method has been developed which will place the tube in the duodenum in twenty to thirty minutes in about 80 per cent of cases where no pyloric stenosis or extensive deforming adhesions are present. I have verified these figures by the use of the fluoroscope in my own cases. A fairly heavy tip such as the Rehfuß or Lyons tip carries the tube down the esophagus through the cardia to a low point on the greater curvature with the patient in the erect position, swallowing about 55 cm. of the tube. After the stomach is washed out, the tip is kept in the antrum near the pylorus in a simple manner by gravity. The patient lies on a couch with the head and shoulders slightly elevated. In this position, there is little tendency for the tip to go back up the lesser curvature. The patient remains in a right oblique position (turned half way toward the right side). This turns the tip toward the right and toward the pylorus.

Then the tube is swallowed *slowly* 15-20 cm. more taking about fifteen or twenty minutes. The tip is moved forward rather slowly by peristalsis through the pylorus into the duodenum and if the tube is fed in fast the upper part travels faster than the tip and loops form in the stomach which often cause delay. It is worse than useless to swallow the tube rapidly or keep feeding the upper part of the tube in unless the tip has gone forward through the pylorus. We need never put the tube in more than 75 to 80 cm.

The type of stomach does not matter much. It is somewhat surprising that the fairly low stomachs are not a real source of delay. Spasm of the pylorus is not important, the slight gagging produced by the tube usually relaxes spasm. We have never used atropin. It is important to know when the tip has passed into the duodenum and when drainage can be begun. This is rapidly and accurately done by the fluoroscope but if the X-ray is not available, a fairly safe estimate may be made in other ways. (1) Inject an ounce or two of air through the tube with a syringe and listen over the epigastrium with the stethoscope. If the tip is in the stomach, we have a low pitched, rumbling sound largely to the left of the median line. If the tip is in the duodenum, we have a higher pitched, hissing sound largely to the right of the median line followed at once by the squirting sounds of peristalsis in the small gut. (2) If the patient drinks a few ounces of water and the tip is in the stomach, it is easily and promptly aspirated out. If in the duodenum it is hard to recover.

For the most accurate diagnostic work, especially if absence of bile is to be used as an important diagnostic point, showing obstruction of the common duct, the X-ray should be used to be sure the tip is in the duodenum and the drainage properly carried out.

THE COLOR CHANGE, THE SEGREGATION OF THE BILE

The average normal sequence of "A," "B" and "C" bile has already been noted and the cause of the color change has already been discussed. In pathological cases this may differ in various ways. The "B" bile may be much darker and more turbid than normal or of different greens and blues or even bloody or there may be no color change to a darker or "B" bile, an absence of "B" bile or there may be an *entire absence of all bile* even with the tube in the duodenum and stimulation properly carried out.

This segregation or separation of the three biles is very far from absolute. It depends largely on color. Sometimes the color change

is sharp and clear, quite often it is slight and gradual and segregation is guess work. I read that "duct bile over 15 cc. suggests duct stasis," etc. I do not believe this is a matter for measurement in cubic centimeters. There is a tendency to say "this is duct bile, this is gall-bladder bile, this is liver bile." As a matter of fact, we have a series of usually open passages all connecting, the stomach, duodenum, common duct gall-bladder, liver ducts, etc., and each bile is usually a mixture. Probably "A" is a mixture of duct, gall-bladder and liver bile with duct bile predominating and "B" and "C" similar mixtures with gall-bladder bile and liver bile respectively predominating. The whole matter of color change and bile segregation needs clearing up. More experimental work on normal animals or men is needed before we can depend upon it to accurately *localize* disease in one specific part of the biliary tract.

The color changes in the same patient are not always constant at different drainages. We naturally expect some variation but the difference may be very striking and capable of various interpretations. It is obvious to me that the gall-bladder or bile tract may be very differently drained in the same patient at different times. Absence of any color change, absence of dark or "B" bile seems important. In the more serious cases, it was commonly found with cystic duct obstruction. This has been several times verified at operation and is a valuable point. I have also seen an absence of "B" bile occasionally in mild cases where it was impossible to believe that the duct was closed. This sign must be taken with the symptoms and other physical signs to be properly interpreted and it is very desirable to repeat the drainage several times on the same patient if it is to be used as an important diagnostic point.

If we are to depend on the absence of "B" bile or of all bile in diagnosis, we must be sure that the tip of the tube is actually in the duodenum. This can be best proved by the X-ray.

THE EXAMINATION OF THE CELLS

The examination of the cells in the bile sediment is important and has also its difficulties. They are best found by picking up the shreds and flakes in a pipette without centrifugalizing and placing them on the slide for microscopic examination. It is important to wash the mouth and stomach very clean so that cells from the bile passages may not be overlaid and mixed with leucocytes and epithelium from catarrh of the nasopharynx, stomach, etc. This is often easy and

sometimes very hard. spurts of gastric contents are often forced into the duodenum before the drainage is finished bringing with them leucocytes and epithelium from above to mix with the bile sediment and also causing a fine cloudy acid precipitate of bile salts. We usually see many extraneous (non-biliary) cells in our slides and sometimes unfortunately the result is like looking for a renal sediment in a case of leucorrhea.

Some experience and skill is needed just as for a urine sediment. Deep bile staining of the cells is usually seen in the true biliary sediments, leucocytes, cuboidal duodenal cells and columnar epithelium from the ducts and gall-bladder.

In normal cases, we may have extraneous cells, few or many, and a scanty biliary sediment, a few leucocytes and round or columnar cells, a few fat needles or fat drops, granular bile salts, etc.

In pathological cases, there may be abundant, deeply bile stained pus cells and desquamated epithelium, columnar and round, mucus, rarely blood cells.

Crystals and amorphous forms of cholesterol and bile salts are always present in some degree. Occasionally they may be very abundant, suggesting the possibility of stone formation. Rarely, there may be a fine, gritty sediment of bile salts. This occurred twice in this series and a diagnosis of probable gall stones was made which was confirmed at operation.

CULTURES

I speak of this subject with mixed feelings. It seems impossible to sterilize the upper digestive tract in any surgical sense and on account of skepticism, the earlier one-half of our cases were not cultured. On the other hand, Cushing, McNeal and Chace and others have shown that the normal duodenum of a fasting patient, is almost free from living bacteria and frequent sterile cultures in chronic cases have shown that contaminations can be often ruled out by the simple measure already described (cleaning the mouth thoroughly, washing the stomach, sterilizing the tube, etc.). The bacteria most frequently found were in this order: the colon bacillus, *Staphylococcus aureus* and streptococci. About one-fifth of the cultures were sterile, a few showed merely contaminations such as *B. proteus* and *subtilis* or *Staphylococcus albus*. There was some real difficulty in deciding whether the bacteria found were causal or accidental and on that account, we have had little experience with vaccines.

Sometimes the cultures were of great value, showing abundant almost pure culture of some pathogenic organism, *Streptococcus hemolyticus*, *Staphylococcus aureus* which matched exactly with the organism found in the tonsil, tooth root abscess or sinus.

More positive cultures were found in acute and subacute cholecystitis and more sterile cultures found in mild chronic cholecystitis and gall stone cases. This is what might be expected from previous cultures on gall-bladders opened at operation. Repeated cultures from the bile drainages of the same patient have proved fairly constant in the well marked cases, and variable in some others.

The bacteria found in the bile drainage cultures have checked up fairly closely with cultures from excised gall-bladder, though less striking than in the interesting and larger series of operated cases reported by Whipple in May, 1921, in the "Annals of Surgery."

DIAGNOSIS

In general, we may say that positive evidence is more valuable than negative and always means disease. By positive evidence, we mean clear signs, such as marked color changes, dark turbid bile, abundance of deeply bile stained pus cells and desquamated epithelium, abundant pure cultures of pathogenic bacteria, a sediment gritty with crystals or such signs as complete absence of bile, or constant complete absence of the color change absence of "B" bile where the drainage is properly carried out and we know that the tube is in the duodenum.

On the other hand, faint or negative evidence does not always mean a normal condition. The diseased area may be blocked off by obstruction as in gall stone cases and other obstructions of the cystic duct and all the drainage come from the comparatively healthy part of the bile passages.

Many chronic cases give sterile cultures.

The diagnosis is easy where the signs are marked, such as dark turbid bile, pus, abnormal epithelium, crystals, abundant bacteria, etc. The diagnosis is not easy and certain in some mild or early or borderline cases in which the method has been emphasized for early diagnosis and early preventive treatment.

There is always the difficulty in judging a new diagnostic method by a long series of "medical" cases in which the diagnosis is only checked in a small portion by operation. We have many of the milder and subacute cases with a clinical diagnosis backed up by the

bile examination, and medical treatment with relief or cure and no absolutely proved diagnosis as we have in a surgical series. Fifteen of our cases were operated and the diagnosis made by clinical symptoms and signs and by means of bile drainage was correct as a rule.

In 10 *normal persons* the bile drainage proceeded in a normal way. There was considerable variation in the color change of the "B" bile. We never found abnormal cells, mucus, crystals or bacteria.

Catarrhal jaundice and cholecystitis cases proved the best group for diagnosis, especially the moderate grade cases without much obstruction. In 38 cases diagnosed cholecystitis or cholecystitis (including many mild and moderate grade cases without operative check on the diagnosis) positive evidence by bile drainage was obtained in 32. In 18 doubtful or very doubtful cases, 14 showed a normal bile drainage. Operative confirmation of both positive and negative diagnoses was satisfactory. In the doubtful cholecystitis cases a normal bile drainage seemed a valuable link in the chain of negative evidence. Several suspicious cholecystitis cases giving a normal drainage showed a normal gall-bladder at operation.

If there was serious duct obstruction, especially of the cystic duct as in acute empyema of the gall-bladder and some chronic fibrous cases the bile drainage test showed little. No bile came from the pathologic area and practically the only sign was absence of "B" or darker bile. If some slight color change was noted, the drainage was not distinctive and fell approximately in the normal class. This same result was found in the stone cases about to be described. In one case of cholecystitis with much obstruction only 6 cc. of bile was obtained but this was so pathological that a correct diagnosis was made.

The gall stone cases were much less satisfactory for diagnosis as a rule unless there was active cholecystitis or the ducts were not obstructed. Of 12 gall stone cases, 8 or two-thirds of the cases gave a normal or approximately normal drainage. The only suspicious feature was the absence or probable absence of darker or "B" bile. This point was especially impressed upon us in several cases where the diagnosis of gall stones was made clearly by X-ray before bile drainage was done and every effort was made by repeated drainage to get a characteristic bile without success. This is easily understood because the ducts especially the cystic duct was commonly obstructed shutting off the chief pathological area from drainage. This may prove to be a very valuable diagnostic point if not simulated in other cases without cystic duct obstruction.

The contents of several excised gall-bladders with stones was studied for sediment and bacteria and were found *sterile* and *without sediment*. The only grossly abnormal feature was the dark ropy character of the bile. This may help explain why some drainages in gall-bladder cases are not distinctive.

In 2 stone cases, on the other hand, a great excess of crystals was found with a distinctly *gritty* sediment and stones were correctly diagnosed.

The cancer cases were naturally a difficult group for study and tiresome procedures. There were 5 cases involving the liver and bile passages (cancer of the head of the pancreas, common duct, gall-bladder). All were deeply jaundiced and in 2, the bile drainage failed due to vomiting or lack of passage of the tube into the duodenum. In the 3 others, there was *entire absence* of bile with presence of pancreatic ferments and more or less blood, a picture very suggestive of malignant obstruction of ducts though, of course, absence of bile may be found in any type of complete common duct obstruction.

In 4 cases of hepatitis, all serious, with deep jaundice, including 1 case of acute yellow atrophy of the liver, the drainage failed on account of vomiting.

The technique of the test is important in diagnosis. Just as in the Wassermann reaction, if the technique is sloppy, the test is useless or worse than useless. Some skill, care and experience are needed. It is easy to be overcritical and say that the cultures are uncertain, the cells dubious and the separation of "A", "B" and "C" bile artificial. It is easy to get discouraged, especially if the first cases are obstructive and no bile is obtained or there is vomiting and it is impossible to get the tube in or stone cases are examined and the bile obtained is not diagnostic. It is better still to give the method a careful personal trial, to recognize its limitations but to get something out of it. If this something is too small to justify the effort, the method will be discarded.

The method in all its detail of preparing the patient, intubing the duodenum, microscopical, chemical and bacteriological examination is somewhat elaborate and time consuming. It is not altogether agreeable. It probably requires an X-ray check for the best diagnostic work, also repetition of the drainage to avoid confusing variation, and it has its limitations. Of course, we do not want any new clinical test unless it is definitely worth the time and expense of using it.

In my own experience, the method has been usually useful and sometimes very useful and I am continuing to use and study it.

To sum up our diagnostic findings in another way, we may say that:

1. Markedly abnormal bile, that is, thickened, darkened bile with an excess of mucus, abnormal cells and bacteria with cultures usually positive (staphylococcus, streptococcus, B. colon) was found in acute cholecystitis and cholangitis and the acute exacerbations of chronic cholecystitis.

2. Slightly abnormal bile that is a clear "B" bile, somewhat thickened with an increase of mucus, few bile stained leucocytes and epithelial cells, usually positive cultures was found in subacute and chronic cholecystitis and a few gall stone cases. In 2 of the latter, gritty bile with an excess of bile salts and cholesterol occurred.

3. Clear, normal bile with viscosity sometimes increased and cultures usually sterile was found in some cases of chronic cholecystitis, most gall stone cases and in normal persons. (Do not miss this. It is unfortunate for diagnosis, but true.)

4. No dark or "B" bile with a clear yellow abundant flow of bile was found in cases of cystic duct obstruction usually due to gall stones (this was several times verified at operation) also in a few mild cases of indigestion in which we do not believe the duct was obstructed.

5. No bile with pancreatic ferments present on repeated accurate drainages was found in common duct obstruction, more frequently cancerous, less frequently due to stone or stricture.

Many of these findings have been confirmed by the extensive experience of Lyon, Whipple, Smithies, Brown, Friedenwald, Sachs and others.

TREATMENT

The treatment of infections of the biliary passages is frequently surgical, but is not always so for example, we do not operate for catarrhal jaundice or many milder types of cholecystitis. All grades of infection are found both as regards severity, duration and the pathological tissue changes which accompany them.

It would be a serious mistake to try medical drainage on acute, urgent, virulent cases, acute or chronic empyema of the gall-bladder, severe obstructive cases which will not drain. On the other hand, there is a real and fairly wide field for medical treatment in the milder

and earlier cases without marked pathological drainage as well as in some doubtful borderline cases in which biliary infections are seriously suspected without being absolutely proved and in which an operation seems too radical. The method is only mildly uncomfortable for the patient and has no danger as far as I have seen or heard.

I believe that the method frequently relieves biliary stasis, will help to clear out infection, will take a load off the liver and, if successful, will frequently prevent more serious damage to liver, gall-bladder and bile passages. It may be tried as Lyon suggested, as an alternate method of treatment where there is a question about the immediate need of surgery and perhaps a supplementary means of *continuing* drainage where immediate surgical treatment leaves the patient only partly cured. It is a matter of judgment where to draw the line between medical and surgical cases. Experience must be our guide. I frankly do not believe that all biliary tract infections need surgery in the early stages any more than all peptic ulcers do. It may be asked: What does this "drainage" accomplish? Is not the bile running off into the bowel every day? All writers agree that biliary stasis in the gall-bladder and ducts is the forerunner of infected gall-bladders and ducts and of gall stones. It is this stasis which the method aims to combat by giving as free drainage as possible. If there were no bile stasis there would be no place for the method in treatment. If we watch results in a group of the milder cholecystitis, choledochitis cases, we see very definite clean cut results within one or two months. We see the jaundice clear up, the bile return to normal in color, cells, mucus and bacteria, the symptoms gradually disappear and health restored. I have definitely watched this sequence in about 20 private patients in the past year and could not fail to be impressed. The drainage was done two or three times a week at the start and gradually dropped to once in one, two, three or four weeks as the case progressed. It has several times happened that the bile has cleared up more slowly than the symptoms and it seemed reasonable to continue the drainages till the bile was normal even after the symptoms were gone, to avoid recurrence.

I realize perfectly that the *method may be abused* in this class of cases, that the diagnosis of mild cholecystitis may be carelessly made and patients, especially neurasthenics, may be needlessly treated by this somewhat elaborate method and may improve in health

because of the strong psychic effect of the treatment in the hands of an enthusiast. It is needless to say that the method should not be used for this purpose alone.

My experience with *catarrhal jaundice* is limited to 6 cases. The group is too small for a definite opinion. The results of treatment were not striking in comparison with untreated cases. Some cases cleared rapidly with drainage. One or two cases in which drainage failed and no bile was obtained, ran a course very similar to those where drainage was done every three or four days. It is worth remembering that an early drainage may fail because of considerable obstruction and later drainages be entirely successful. The treatment seems logical and we are prepared to try it further.

Even in some inoperable gall stone cases, it is apparently possible to get results with duodenal drainage. I have been forced to try this treatment, not from choice, but from necessity in 2 patients with gall stones. Both had typical biliary colics, in both, the stones were clearly and beautifully pictured by X-ray and both were considered bad surgical risks because of angina or chronic nephritis. In both cases the treatment was begun just after a series of severe colics and in the presence of jaundice and as a result or sequence of biliary drainage, all gall-bladder symptoms disappeared, the stones became entirely "latent" and have remained so for more than a year and the patients consider themselves well as far as the gall-bladder is concerned. Of course, this is not a plea for the use of medical drainage in gall stone cases, but merely a record of a surprising result or sequence of treatment in 2 inoperable patients.

I may add that I have reluctantly tried the same treatment for a short time in a few stone cases at the urgent request of the patient, who dreaded operation and was anxious to try any method which gave the slightest hope of medical relief. No gall-bladder bile was obtained, the cystic duct was obviously obstructed and the patients came to operation as might be expected.

The use of vaccines is logical in infections of the biliary tract as in any other type of low grade infection where the system is unable to produce sufficient antibodies to destroy the bacteria. We have found much difficulty in verifying a particular organism as the source of the infection and on that account, have used vaccines in only a few cases.

SUMMARY

The profession owes Meltzer and Lyon a debt for their stimulation of the study of the liver. They have made us think and have given us a new method.

The early papers seem over-enthusiastic and dogmatic and said too little about the limitations and difficulties of the method. We cannot agree with them in detail.

The physiology of the method, the cause of the color change, the action of MgSO_4 on the gall-bladder, the segregation of the bile need further study in normal individuals or animals to give a firm foundation for clinical and diagnostic work.

Its use for diagnosis has its difficulties and limitations. It is somewhat elaborate and time consuming, consisting of intubation, lavage, aspiration, microscopical examination, cultures, etc., but it can be carried out on nine-tenths of the patients chosen for examination. It requires repetition of the drainage and also the use of the X-ray for the best diagnostic work, although much diagnosis and most treatment can be done without the X-ray. The segregation of the bile, the study and interpretation of the cells and bacteria present difficulties most of which can be overcome by experience. The pathologic area may be blocked off by obstruction, e.g., of the cystic duct and the drainage not be very abnormal in an important case.

In spite of these limitations, the method has proved useful and sometimes very useful in diagnosis.

It helps to show whether the ducts are open or closed. If no dark or "B" bile is obtained on repeated drainage, properly performed, we may suspect cystic obstruction, frequently with gall stones.

If *no bile* is obtained with a proper drainage but pancreatic ferments or blood are found, common duct obstruction is present, frequently malignant.

Cholecystitis and cholangitis cases, unless marked obstruction exists usually give a bile which is abnormal in color, appearance, cells, mucus and bacteria.

Gall-bladder sand may aid in the diagnosis of gall stones, but in general, the drainage in gall stone cases was not characteristic.

In treatment, it is logical to combat biliary stasis, the well recognized forerunner of biliary catarrh, infections and stones. We are not sure at present how completely this method empties the biliary passages in all cases, but in many it appears to do this very well.

The best field for use is in the milder and moderate grade of cholecystitis and choledochitis cases where no marked obstruction exists. Many such cases are greatly relieved or apparently cured following this treatment.

It is obviously unsuited for treatment of acute, virulent infections of the gall-bladder, acute or chronic empyema, gangrenous cholecystitis or cases with known stones or tumor, or severe chronic obstructive cases which will not drain. It may be occasionally useful in some of these cases when surgery is contraindicated, as in old people, or in cardiac, renal or diabetic patients.

In closing, I wish to acknowledge my indebtedness to my colleagues at the Boston City Hospital for the opportunity to study their patients and to my co-workers, Doctors Resnick, Burger and Sharpe for their valuable assistance.

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BILIARY-TRACT DISEASE PERSISTING SUBSEQUENT TO OPERATIVE PROCEDURES, AS REVEALED CLINICALLY AND BY METAPYLORIC ASPIRATION (MELTZER-LYON METHOD); A REGIMEN OF TREATMENT

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One of the most important clinico-pathologic observations of the past decade has been that but rarely (e.g., malignancy, congenital and circulatory structural faults), does gall-bladder disease represent of itself an essentially primary ailment. Gall-bladder malfunction has been shown to be largely a consequence of acute or chronic infective processes, during the course of which bacteria are carried to and lodge in its wall. Such bacteria travel to the gall-bladder through the blood and the lymph streams, and, frequently from far distant primary foci. The secondary gall-bladder bacterial colonization may remain active and harmful long after the initial acute ailment or chronic disease has subsided or has been eradicated. Only infrequently does a gall-bladder wall become diseased from abnormal gall-bladder contents; the abnormal content of the viscus commonly represent bile-admixed by-products of the existing process of destruction and an attempt at repair going on in the gall-bladder wall. Consequently, study of gall-bladder contents, macroscopically, microscopically and culturally not infrequently discloses the nature and the pathologic degree of the lesion in the wall.

As one of us (Smithies (1)) showed more than five years ago, by a study of 1000 operatively demonstrated instances of gall-bladder disease, smears from freshly secured gall-bladder biles exhibited infecting organisms in 28.6 per cent of cases but cultures from these returned growths in rather more than 63 per cent of specimens planted. The organisms recovered upon culture were of groups similar to those of the primary infection to which the gall-bladder lesion reasonably might be considered secondary.

Ranking in importance with the proof that gall-bladder disease usually is secondary to blood- or lymph-streams borne infection, is the more recent clinical and pathological observation that only few

instances of gall-bladder disease exist which are not associated with disturbances in other segments of the biliary tract, the common and hepatic ducts, the bile capillaries in the liver, and, as McCarty (2) of the Mayo Clinic has recently demonstrated, lesions (often of undoubted function-hampering degree) in the liver itself.

Further, it has recently been recognized that, concomitant with chronic biliary-tract disease, serious damage in alimentary tract function may exist. Particularly, may be impaired the secretory capacity of the stomach and the pancreas. In the series of gall-bladders above referred to (1), gastric achylia was observed in 20.9 per cent of the cases. Such anomaly demonstrates how commonly the dyspeptic disturbances present with gall-tract disease may be due to extra-biliary malfunction. In our cases, grossly enlarged, infected lymphatic glands were exhibited by 12.4 per cent, chronic pancreatitis in 6.3 per cent (28 per cent of the pancreases were grossly enlarged in instances of common duct stone and 17 per cent in cases of simple chronic cholecystitis); there was acute pancreatitis in 2 cases and, of the series, deficient pancreatic function was proved in more than 8 per cent of cases studied (Gross-Fuld-Wohlgemuth method).

From the above, it is quite evident why physicians, who perform surgical procedures upon the gall-bladder, have for so many years engaged in bitter controversy with respect to which procedure gave the better results, chiefly, *cholecystectomy versus cholecystostomy*. Even ancient knowledge of the abdominal pathology concomitant with gall-bladder disease, would appear to indicate why neither cholecystectomy nor cholecystostomy could prove an entirely satisfactory operative procedure in a considerable group of patients, inasmuch as neither procedure could repair damage already experienced functionally and histologically by the stomach, pancreas and liver.

Our recent report (3) upon the diagnostic and therapeutic value of non-surgical biliary tract drainage after the intra-duodenal introduction of magnesium sulphate solutions as suggested by Meltzer and by Lyon, would appear to offer a practical guide to the careful surgeon with respect to operative procedures upon the gall tract. Certainly the surgeon of the future must consider gall-bladder disease not as an entity, but must think of a diseased gall-bladder as a localized, get-at-able and removable portion of what is commonly a wide-spread and frequently, progressive pathologic process. Metapyloric, diagnostic biliary-tract drainage indicates, practically, to the surgeon whether the gall-bladder is alone at fault (in which event, cholecystec-

tomy appears indicated), or, whether the gall-bladder is diseased concomitantly with the common and hepatic ducts and the bile capillaries in the liver (in which event cholecystostomy with long continued drainage would seem to be a suitable procedure).

While the future course of biliary-tract surgery would appear to be mapped out, fairly logically, and while our studies upon non-surgical biliary-tract drainage have shown that many gall-tract affections can be taken care of satisfactorily without surgery, yet, today, internists have to deal with a great group of patients who have had more or less haphazard surgical procedures performed upon the gall tract in the past years. While the operative mortality of gall-tract surgery has not been especially great (rather more than 5.5 per cent in the average, first class clinic), any one with experience knows that the digestive morbidity of such patients is very high. There are, indeed, very few individuals upon whom cholecystectomy or cholecystostomy has been performed, who, five years after operation, are free from digestive malfunction. The internist meets these patients more frequently than does the surgeon because, since they have had all possible surgery performed, they seek relief from him rather than go back to the surgeon.

Clinically, such patients experience distress in the liver region, frequently with definite enlargement of the liver; annoying feelings of "up pressure" particularly at night, and often associated with cardiac disturbances; belching of gas, eructations; constipation or periods of diarrhea alternating with constipation; distension of the intestines; chronic, moderately severe anemia, sallow skin and frequently asthenia. Occasionally, acute exacerbations occur, with severe pain in the liver and gall-tract regions, and at times, transient or persistent icterus. Irregular recurrences of temperature are not infrequent. The blood analysis usually demonstrates a mild polynuclear leucocytosis; gastric secretion is deficient; pancreatic insufficiency and intestinal indigestion with putrefaction may occur.

Until recently, the treatment of these patients has consisted largely in mapping out a theoretically ideal diet, and the exhibition of "digestants," "cholagogues," so-called "tonics" and purgatives. Certainly, there has been need of more direct action, therapeutically, in this group of unfortunates. During the eight months in our routine work, there have come to us 14 patients in rather grievous condition, who had been subjected to biliary-tract operations, but who subsequently, had not recovered health, strength or normal digestion.

Surgically, nothing further could be done; therefore, in an attempt to give them relief, we have instituted non-surgical, biliary-tract drainage metagastrically. This preliminary report deals with our experiences in this class of patients.

The 14 patients reported are taken, consecutively, from our records between September 8, 1920, and April 29, 1921. There were 12 women and 2 men. During this period, we carried out metapyloric drainage upon 309 individuals, 600 times—an average of rather less than 2 drainages per person. These 14 post-operative cases underwent a total of 57 drainages, more than double the common average. To emphasize the nature of the problems presented, one case is summarized briefly; the remainder will be considered as groups.

ILLUSTRATIVE CASE

Mrs. M., the wife of a prominent central Illinois surgeon, from early childhood had experienced frequently recurring attacks of pain in the right upper abdominal quadrant; these attacks usually were associated with fever. At age of thirty-two, icterus developed; it continued six weeks. Following the icterus, seizures became more definitely characteristic for gall-tract disease, and obstructive signs later appeared; at age forty-three, the gall-bladder was removed by Dr. W. J. Mayo, at Rochester, Minn. The pathologist's report was "strawberry" gall-bladder and a single, large stone. Immediate, post-operative convalescence was rapid; the patient returned home in good shape, but in a few weeks developed a recurrence of acute right upper abdominal symptoms of so alarming a type that she was hurried to the Presbyterian Hospital, Chicago. Dr. J. Clarence Webster reopened the abdomen and evacuated about a pint of pus from beneath the liver. Convalescence was stormy; subsequently stab drainage was required; the patient left the hospital in about one month. For a year she lived in fair comfort, then attacks of severe pain at the right costal margin became troublesome and there were associated periods of transient jaundice and clay-colored stools. A second trip to Rochester was made. It was advised that further operative procedure would be unwise. Under strict dietetic restrictions there occurred temporary improvement but the patient did not remain free from severe pain and dyspepsia. On November 3, 1921, she was brought to us for study.

Her physical examination disclosed, among other anomalies, a liver, enlarged, smooth, not pulsating or tender; definite muscle spasm over the site of the common bile-duct and the head of the pancreas; the shoulders and small joints of the fingers exhibited early peri-arthritis; there were patches of psoriasis over the trunk and extremities; the tonsils were enlarged, pus was present in small amount in the right and there was a low-grade infection of the sinuses accessory to the nose. Double tonsillectomy was advised (and performed) and repeated drainages of the biliary-tract, per duodenum were instituted.

Results from the metapyloric drainages. At the first drainage, only 125 cc. of thick, turbid, dark yellow bile were secured; it contained many flocculi, with a considerable admixture of pus; bacteriologically there was recovered an abundant growth of

colon bacilli. At the *second drainage*, the congestion and swelling in the mucous membrane of the biliary passages had become so reduced that we were able to secure 500 cc. of bright yellow bile, exhibiting a heavy sediment of pus, erythrocytes and cholesterolin crystals. There was a strong musty odor to the bile recovered; on culture, a growth of staphylococci and colon bacilli was secured. At the *third drainage* about 120 cc. of clear, bright, lemon-yellow, normal-appearing bile was spontaneously discharged upon the introduction of the duodenal tube (apparently the contents of dilated common-and-hepatic-ducts) and after the instillation of magnesium sulphate, this was followed by a second lot of 180 cc. turbid, brownish-yellow, thick bile (seemingly liver bile) with a rather light flocculent sediment, containing blood and pus cells in lesser amount, with a less exuberant bacteriological growth, again staphylococci and colon bacilli. The *fourth drainage* yielded only about 200 cc. of one-type bile, with a heavy sediment; it contained but little pus, but a massive culture of colon bacilli with a slight admixture of *Micrococcus catarrhalis*. At the *fifth session* 400 cc. of thick, turbid lemon-yellow bile was discharged spontaneously, during a period of about four hours before any magnesium sulphate was given. Administration of the salt was followed by prompt, profuse flow of 250 cc. bile, having much the appearance, although not the odor, of rotten eggs and later, a third portion of 700 cc. of somewhat thin and watery, turbid light-yellow bile. This totaled, for the seance, 1350 cc. and was the largest amount secured from this patient. At our *sixth drainage*, 480 cc. were obtained—half spontaneously, half after the magnesium sulphate was administered intra-duodenally. Both lots were thick, turbid, opaque, of syrupy consistency, with heavy flocculent sediment and tiny, macroscopic blood clots. Bacteriologically, a few colon bacilli were present in pure culture; microscopically the sediment was chiefly amorphous bile salts with but little pus.

Following the drainages, physically, the patient exhibited marked improvement in general well being; the liver enlargement subsided so that the organ could not be palpated. After the sixth session, the patient's husband took charge of the drainages at her home. We learn from the Doctor that the marked clinical improvement which set in after the first biliary-tract drainage still continues; in fact, the patient regards herself as well. The drainages, by us, were carried out over a period of seven weeks.

ANALYSIS OF MATERIAL STUDIED

In this patient, as in others of our series, metapyloric drainage has afforded a way of emptying the dilated, distended, infected biliary passages from the papilla of Vater to the finer hepatic radicles, such as was in no other manner practicable, in an individual who was rapidly becoming a helpless invalid due to definite evidence of spreading malfunction (exhibited by chronically enlarged liver, biliary-tract stasis, gastric and intestinal indigestion, abdominal pain, early arthritic changes and general undernourishment). Such distressing state occurred in spite of the efforts of conservative surgeons of great experience and skill, and in spite of dietetic, hygienic and medicinal

regimens suggested by competent internists. We are not familiar with any alternative procedure, surgical or medical, which offers such persons as this unfortunate woman as much relief as did metapyloric drainage of the biliary tract after the method of Meltzer and Lyon. It would seem to be proved that there is now available, therapeutically, a fairly certain, quick, easy, painless, safe form of relief, without the necessity of the subject's entering a hospital or of leaving home (the cases quoted in this report were ambulatory patients). The only interference with normal avocation is part of a day's time for each drainage.

In summary, our 14 post-operative cases, upon which non-surgical, meta-pyloric biliary-tract drainage was performed, are classed as follows:

a. Surgical procedures. Whenever possible, we have confirmed by conference with the operator, the nature of the original operation as reported to us by the patient. In 2 cases, this was not possible, but the existence of at least a gastro-enterostomy was confirmed by fluoroscopy. These 2 patients were our least satisfactory cases; they are included for what they are worth and to emphasize some of the difficulties presented in handling this post-surgical group.

b. The patients' health in the interval between operation and metapyloric drainage. It is undoubtedly within the experience of each of us that many patients subjected to interference with biliary-tract integrity, by operation, fail to secure any considerable benefit from such procedure, either immediate or ultimate; also, that a number receive amelioration of symptoms, but after an interval, relapse into a condition closely analogous to that existing when they first sought surgical aid; and finally, a third lot considers itself to be, and in fact, seems to be, clinically well, when judged by external and subjective evidences.

Only recently, the publication of the studies of Widal, Abrami, Birsaud and Iancoresco, on the nature of shock and the significance of hemoclasia has furnished us with a simple, and seemingly dependable, method of estimating the degree of functional capacity of the hepatic cells. It would appear to be a necessary part of the routine of examination of liver and biliary-tract patients, that hemoclasia be estimated; certainly this should be done for all cases before biliary-tract operation and after such previous to their discharge from medical supervision. Tested for hemoclastic shock, the 1 case in our series

reporting continued good health after a cholecystectomy performed four years previously, exhibited the greatest percentage of decrease in hepatic function which we have noted in any of the patients upon whom we have performed the test. Subsequent to the administra-

TABLE 1
Nature of operation

OPERATIVE PROCEDURE	PATIENTS	NUMBER OF CASES
Cholecystectomy	Mrs. S., Mrs. C., Mrs. D., Dr. G.	4
Cholecystostomy	Mrs. L., Mrs. G., Mrs. S.	3
Cholecystectomy with gastro-enterostomy	Mr. P.	1
Cholecystectomy with second operation for adhesions	Mrs. W.	1
Cholecystectomy in two stages	Mrs. M.	1
Cholecystectomy with secondary drainage, local abscess	Mrs. Mc.	1
Some form of gall-tract operation with gastro-enterostomy	Mrs. K., Mrs. G.	2
Operation on gall-bladder	Mrs. D.	1
Total.....		14

TABLE 2
Summary of patient's health between time of operation and of drainage

CONDITION	PATIENT	NUMBER OF CASES
(a) Not improved	Mrs. K., Mrs. G.	2
(b) Improved, but still impaired	Mrs. Sh., Mrs. Wa., Mrs. Ca., Mrs. Ga., Mrs. De., Mrs. Mc., Mrs. Sm., and Mr. Pi.	8
(c) Improved temporarily, now worse	Mrs. Li., four years, Mrs. Mo. (eight years), and Mrs. Do. (four years)	3
(d) Considered self well, but hemoclastic shock present	Dr. Gi.	1
Total.....		14

tion of his proteid meal, this patient's leucocyte count fell 1925 in forty minutes and still showed a leucocyte deficit of 1600 after one hour and forty minutes. As exhibiting an interesting side light upon

the clinical possibilities of an impairment of hepatic function, we may mention that this patient, a Louisiana physician, sought relief from persistent weakness, with tachycardia; a diagnosis of "obscure hyperthyroidism" had been made, but his basal metabolic rate showed so marked a fall below the normal as to render such diagnosis untenable (minus 21.08 per cent, average of three tests).

b. Results of biliary-tract drainages. It may be of interest to particularize upon the results of the drainages. As might be expected from the nature of our cases, e.g., patients with toxic states persisting for long intervals prior to their coming to us with biliary passages usually clogged with thick tenacious mucus, and membranes lining the ducts, swollen and congested, the least satisfactory results were in the patients who underwent the fewest drainages (3 or less) or who were drained at long intervals; the best results were secured in those

TABLE 3
Results of metapyloric drainage

(a) Successful drainage with marked clinical improvement.....	6
(b) Successful drainage with limited clinical improvement.....	3
(c) Successful drainage, but patients did not return for subsequent treatment..	2
(d) Drainage in absence of clinical symptoms, hemoclastic shock being present.	1
(e) Drainage only partially successful—slight clinical improvement.....	1
(f) Entire failure of attempts at drainage—no clinical improvement.....	1
Total.....	14

patients who were drained frequently. It is our opinion that 1 or 2 drainages are required in this type of case in order simply to render the bile passages patent and thus to open a way for the discharge of thickened, static, infected bile from liver-duct ramifications. This begins to appear in large amounts at later drainages. We believe that some of the less favorable results reported by other observers using this method, are due to a lack of persistence in its application beyond a first or second session, and especially, *to not devoting sufficient time and care at each drainage*. We know this to be a fact by our early experience and by observing the work of others. It is our custom to advise each patient that the procedure will probably consume the greater part of a day; we continue the seance well into the late afternoon if satisfactory results are not earlier secured. Some of our most striking successes have been attained after 4 p.m. of a seance which began at 9 a.m. Of course such drawn-out sessions are

the exceptional—the ordinary duration of a drainage consumes much less time.

Number of drainages required in each group: Those patients exhibiting marked clinical improvement were 6 in number; they experienced a total of 41 drainages or an average of nearly 7 *drainages each*. There were 3 patients who had successful drainages, but who showed limited clinical improvement; they had a total of 7 drainages or an average of approximately 2 *each*. Two patients upon whom the first drainage was successful and therapeutically promising, gave us no opportunity to follow their course. The symptom-free physician with tachycardia, who had been classed previously as "Grave's disease," improved definitely after 2 drainages, but still exhibits hepatic dysfunction, as demonstrated by hemoclastic shock.

In the gastro-enterostomized patients, we were not able to secure satisfactory biliary-tract drainage, in two attempts upon each, and therefore could not lay claim to being of any particular service; this observation upon such patients may prove of value to other physicians in their work. The complicating factor in these patients was the presence of a gastro-enterostomy opening so large, and so situated anatomically, that the duodenal bulb constantly tended to enter the jejunum; magnesium sulphate discharged into the jejunum seems to be entirely inert, so far as our experience goes, in the activation of the biliary response usually secured upon its metapyloric instillation.

d. Nature of bile secured in later drainages compared with the earlier reactions. When practically normal bile was finally secured, clinical improvement coincided in 2 patients. There was 1 patient where bile, practically normal, was finally secured but the clinical improvement was slight; this seemingly due to the presence of old pericholedochitic adhesions. Clinical improvement was marked in our patient in whom the bile was never badly infected; such improvement would seem to follow the mere elimination of biliary-tract and liver stasis. That such factor is of great importance is shown by the very marked clinical improvement occurring in 3 of our patients, from whom we still secure bile specimens exhibiting bacteria and products of infection. In 2 other patients, however, physical and symptomatic improvement appear to be progressing directly as evidences of infection disappear from the bile-tract fractions. And, it is interesting to note that in such cases hemoclastic shock is likewise becoming less pronounced. We can, of course, report with no reliability, progress, clinically of patients whom we drained but once (3) or upon whom drainage was not regarded as being successful (1).

e. Clinical results summarized. Clinically considered, omitting the case without symptoms, those who did not return, and the case wherein we were not able to pass the bulb into the duodenum, the 10 remaining all show definite improvement, varying from a lessening of the number and frequency of attacks of pain and dyspepsia, gain in weight, improved digestion and elimination, improvement in or restoration of blood to normal, to an apparently complete clinical and subjective recovery. Some patients are so strikingly improved and in so short a time that unless their course had been observed, recital of their progress would not obtain credence.

In closing, it should be said, in all fairness to our surgical colleagues, that, of course, it is not those patients who have secured relief from their troubles by operation who are still drifting from one physician to another, with biliary-tract morbidity. We are dealing in this series with a group of difficult cases. We cannot too strongly emphasize the fact that these people have already received the benefit of all possible surgical procedures and, until recently, always have been dismissed with prescriptions for purgatives, cholagogues and with dietetic instructions. Both surgeons and internists have been at a loss with respect to further treatment; the infection has passed to an anatomical location where the knife cannot be used with safety and where medicinal agents are but therapeutic gun-shots. Our experience, added to that of Lyon, Crile, White, Friedenwald, Sachs and many others, has definitely shown that this method offers a direct way of ridding the liver and the biliary passages of stagnant, infected bile in addition to its offering practical aid in the diagnosis of gall-tract disease. It is admittedly a new procedure; we do not for a moment pretend that we have more than touched upon its possibilities; we merely offer this report of our results in a small group of cases for consideration in the hope that other clinicians will be interested in what we regard as one of the most promising of those procedures developed through the assistance of applied, clinical physiology and pharmacology.

Our experience would lead us particularly to emphasize the necessity in treating these post-operative cases, of pushing the drainages energetically from their inception. Such would appear urgent in order that the bile passages be quickly cleared of thick mucus and accumulated inflammatory debris and in order to establish early, free, hepatic secretion. Drainages should be repeated every four or five days at least (perhaps oftener), until a bile is secured which ap-

proaches normal, quantitatively, chemically, cytologically and bacteriologically. These drainages require time and patience. The subject never should be hurried; an atmosphere of leisure and accommodation should be created; often an entire day will be consumed in a single drainage. So conducted, the procedure will prove without annoyance to the patient; he readily coöperates respecting frequent drainages as, subjectively and objectively, improvement occurs.

In the rooms where drainages are being conducted, or at least in some quickly accessible spot, there should be microscopes for the cytological and bacteriological examination of fresh specimens; suitable stains must be available; reagents convenient, and culture media should be at hand so that implants may be made at once that later may be worked out the bacteriologic picture. In severe biliary-tract infections, particularly those originating from streptococci or certain strains of colon bacillus, facilities should exist for the preparation of suitable autogenous vaccines.

Following a drainage, proper regimen should be established in every case. We suggest to our patients a diet low in fat and in protein. Each patient is given a typed sheet of instructions in this regard. Such diet gives the liver all possible physiological rest. At this time, when the ducts are comparatively patent and free from accumulated, pathological bile, some drug may be administered with the object of aiding in combating infection of the duct and the gall-bladder walls. Sodium salicylate has been found to be most satisfactory, when given in sufficient dosage to saturate the infected tissues; particularly does it seem useful where coccus infections of the rheumatoid type are present. After the expiration of thirty-six hours, the patient is gradually allowed a more generous diet, but its fat and protein content should be kept relatively low for months, even after convalescence and evidences of normal liver function seem to be well established.

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DISCUSSION

DR. JOHN A. LICHTY, Pittsburgh: I will only present the evidence which we have from our own clinic in the Mercy Hospital. It is rather from a diagnostic standpoint than from a therapeutic standpoint. I do not wish to enter into the discussion of whether the magnesium sulphate is necessary in the technique or whether the gall-bladder contracts, or what happens. We have at the Mercy Hospital drained something over 100 biliary tracts. The first 20 cases were not so satisfactory because the work was new to us. But of 83 cases carefully studied, 21 were operated. The Lyon test was confirmed at the operation in 18 of these. Now, of these 18, 14 were cases in which we had no "B" bile, and in these 14 there was either a stone in the cystic duct or the gall-bladder was distended, full of stones. We had 3 cases operated in which "B" bile was absent but in which we found no definite pathology other than a cholecystitis. After that we became more diligent in our tests and when "B" bile was absent we repeated the test a number of times before we concluded it was not obtainable. We found we had not been persistent enough to get "B" bile.

I wish only to say, whether there is any good in this procedure or not, whether it is reliable from a diagnostic standpoint or whether it has scientific value or not, it does seem to help us to bring patients to operation who should be operated, easier than where we do not make the test. The resultant confidence which the patient manifests after a careful study by this method makes it worth while.

Of the 83 cases studied, 21 were operated. This could not have happened before we did the Lyon test. We have had many cases which should have been operated, but were not because we seemed to lack some element of certainty in our diagnosis. From our work we feel that we have not had any patients operated where the operation was not justified and should not have been done.

DR. CLEMENT R. JONES, Pittsburgh: I would like to relate my experience in 1 case in particular in which we were unable to obtain the specimen of "B" bile. And instead of "B" bile we were able on the second introduction of the magnesium sulphate to secure a small quantity of white mucus tinged with green which we might describe as a verdigris green. This mucus was very characteristic in all the drainages which amounted to about 75. I had nothing which approached that character of the mucus coming from the duodenum. Then we had several other drainings three days apart and were unable to secure another like specimen of mucus. The patient had a frank gall-bladder colic two weeks later and came to operation. When the gall-bladder was removed, I opened the gall-bladder and found a teaspoonful of the same type of mucus with the same peculiar green tinge with a stone the size of an olive stone in cystic duct which had produced occlusion.

DR. WILLY MEYER, New York: I listened with keenest interest to Dr. White's paper and also to the papers of the other colleagues just read. Dr. White stated that in the cases in which he did *not* get the bile as seen in the Meltzer-Lyon test the surgeon usually found a stricture of the cystic duct at the operation. To show how we are really in the very beginning of this interesting observation and investigation and must all learn a great deal before we can make definite conclusions, let me cite the case mentioned before by Dr. Einhorn, that of large stone in the

cystic duct. There we had had the entire normal cycle of the magnesium sulphate test, and yet the cystic duct was blocked by the stone completely, and on incising the extirpated gall-bladder we found a bloody *brown* fluid entirely different from that black bile which had been obtained at the time of the examination done one day previous to the operation. These observations show, as I have just mentioned, what different results we may obtain and how much more we must learn to properly estimate the results of his test.

In the fasting condition we frequently had the color of pea soup, just the same fluid which we found later in the gall-bladder on cholecystectomy. There is not the slightest doubt that in the fasting condition the gall-bladder empties itself; and if it does not do so, the instillation of a few cubic centimeters of a warm saline solution into the duodenum will suffice to make the flow appear.

In conclusion I beg to call attention to an article which is to come out in print very soon, written by Dr. Garbat, the serologist of the Lenox Hill Hospital, New York, for which he received the Cartwright prize from Columbia University. It covers the investigations made by him while in military service; Dr. Garbat brings out what Dr. Smithies has just mentioned, viz., that the infection in a great many instances not only affects the gall-bladder, but the entire biliary tract. But do not let us forget that the gall-bladder is an extirpable cavity and that man can well get along without it. If the surgeon has removed it because it was infected and diseased, he has done, I think, a great service to the patient. We have seen it over and over again, and the Mayo Clinic published similar observations several years ago, that the gall-bladder wall contains bacteria, while the bile within it may be found perfectly sterile. But it stands to reason that these bacteria in the gall-bladder wall will enter the gall-bladder cavity now and then, and infect and reinfect its contents. The proof of this truth, to my mind, is given by the fact, found by Aschoff, that the center of gall stones so very frequently show the presence of bacteria. The surgeon removes the gall-bladder on account of its being a focus of chronic infection. Should the patient exceptionally still remain diseased, likely on account of, call it, a subacute cholangitis of mild character, the foundation for improvement at least has been laid. If now this treatment with magnesium sulphate instillation into the duodenum is carried out by the medical man, the patient can rightly entertain the hope to be completely cured by the addition of this new and splendid method.

DR. JULIUS FRIEDENWALD, Baltimore: In the first place, I would like to say that I have had two young men working on animals in this sort of work, but results are not complete; but two things are settled—one is that magnesium sulphate does produce a flow of bile, and the second, that a bile to be infected need not be dark. We have infected a gall-bladder and have obtained the same organism in bile which was perfectly clear.

Now in regard to Dr. Smithies' paper, I should like to state that I have had quite a number of cases who have gone through the same experience, who have had their gall-bladders drained and gone through this—one patient operated on by Dr. Mayo and the patient continued to suffer, and in quite a large number of these cases the patients have been relieved notwithstanding the fact that they have had months and years of pain. I think there is no better method of showing that this plan of

treatment is a good one than by citing this class of cases, and there is no other means of relieving them, not even surgical means.

DR. FRANKLIN W. WHITE, Boston (closing): We occasionally find an absence of darker bile, a lack of color change, a persistent drainage of light or golden yellow bile. If we use this as a diagnostic sign it must be reasonably constant in repeated drainages of the same patient. In the more serious cases it is often found with a blocked cystic duct, but it cannot be emphasized as a diagnostic sign of this condition unless there are other characteristic local signs and symptoms, for there are many mild cases where there is obviously no cystic duct obstruction which give only a flow of light yellow bile.

DR. FRANK SMITHIES, Chicago (closing): We must think not only of mechanical factors with regard to the gall-bladder emptying but of "physiologic block." I think that last is of far more importance than the first. You have a diseased area which under normal circumstances responds to normal stimuli. It may not be able to respond to abnormal stimuli in whole or in part; it may be that this physiologic block acts on the gall-bladder and causes it not to respond unless it is relieved of the load, even when its ducts are patent. We see a similar condition where distension of the urinary bladder exists or where following catheterization there is atony and inability to perform its normal function of contraction. These cases of physiologic block are most important with respect the gall-bladder; we may have only partial emptying and so, at different seances we may get different biles, accordingly as the nonstriated muscle of the gall-tracts respond to stimuli in varying degree. We have seen manifestations of this phenomenon over and over again.

With regard to Dr. Meyer's remarks, I am interested to receive such words from a man who has done such an amount of conservative surgery. It is rare to have that surgical attitude toward this sort of thing, and yet it is highly beneficial; we must not forget, however, that the removal of the gall-bladder interferes with the normal physiological chain and, consequently, with normal response to stimuli. I have seen in Dr. Ochsner's clinic cases reoperated upon where the common duct held more than the contents of a normal gall-bladder and we have seen hepatic very large ducts passing up into the liver, greatly dilated beyond where we could trace them. In many of these individuals there were visible evidences of stagnant bile far up in the liver. We must not forget that these abnormalities which are not disclosed by Lyon represent evidences of disease and not due to liver excretion of magnesium sulphate. It is true that a response will occur to water or other solutions, but it is also true that it occurs more readily when there is contraction of the smooth muscle fibers in the liver itself to solutions of magnesium salts. Doyon proved the physiologic sequence of these responses long before Meltzer worked with magnesium. Magnesium sulphate is an inexpensive and usable drug, but we must learn how to use it as a dependable method of routine; after a reasonably long period of careful work we now think that we have reached the point where we are able to get something dependable from what we are doing.

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